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THE SIGNIFICANCE OF EXPERIMENTAL TUMOURS FOR HUMAN TUMOUR CAUSATION.[1]

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THE object of this discussion is not to review the vast amount of experimental work on the induction of tumours which has been carried out during recent years, but to survey broadly the various experimental results from the point of view of whether or not they have their counterparts in man. We now know a great many chemical substances and other agents which have been proved to be potent carcinogens in animals, but which have not been incriminated as the causes of any tumours in man; and we are able to induce tumours experimentally by introducing carcinogens directly into tissues to which they can have no direct access in man. Of what significance are such experimental results? Are any of them pointers to some of the undiscovered causes of human tumours?

What I can say in a short discussion is necessarily sketchy and selective. For further details and references, I recommend the many excellent reviews in Volumes IV and XIV of the *British Medical Bulletin* (1947 and 1958) and in Volume I of "Cancer" (edited by R. W. Raven), and those of Hueper (1954) and Badger (1956).

[1] Read at the Cancer Congress of the Anti-Cancer Council of Victoria on August 22, 1960, at Melbourne.

The Carcinogenic Hydrocarbons.

Carcinoma of the Skin.

It is now common knowledge that the first recognized occupational tumours—chimney-sweep's cancer, cotton-spinner's cancer and cancers of the skin in tar and oil workers—were caused by carcinogenic polycyclic hydrocarbons. This was revealed by the classical researches of Kennaway and his co-workers in the late 1920's, which culminated in the first identification of pure chemical carcinogens and the proof that the chief of these in tars and oils was benzpyrene. The experimental skin cancers produced in rodents by the pure hydrocarbons are thus strictly analogous to the tar and oil cancers of man. Of great significane also was the discovery by Kennaway and his team that potent carcinogenic tars can be obtained artificially by heating almost any organic matter to charring temperatures, in which process benzpyrene and other carcinogenic hydrocarbons are generated. In the light of this discovery we can understand the presence of these substances, not only in coal-tars, lubricating oils and soot, but also in many other materials which have been artificially heated during their manufacture; for example, benzpyrene has been demonstrated in processed rubber (Falk

et alii, 1951), in smoked meat and fish (Bláha *et alii*, 1949; Bailey and Dungal, 1958) and in cigarette smoke (see below).

Ingested Carcinogens and Alimentary Cancers.

Many kinds of visceral carcinomas, including alimentary ones, can be produced by the direct local injection of carcinogenic hydrocarbons into various solid organs or into the walls of hollow organs. But such local injection of concentrated carcinogens into tissues is a very artificial procedure and probably has no counterpart in human carcinogenesis. However, in the alimentary and respiratory systems, it is, clearly, very probable that the continuous ingestion or inhalation of carcinogenic substances may well be largely to blame for the all-too-common cancers of those systems.

With regard to the alimentary canal, the comparative pathology of tumours is surely of great significance. While gastric and intestinal cancers are amongst the commonest in man, they are rarities in all other species. This very striking difference may well be the result of our culinary methods; frying, roasting, grilling and toasting subject many kinds of organic substances to nearly or actually charring temperatures, which, as Kennaway and his co-workers showed, may produce carcinogenic hydrocarbons. The great differences in the incidence of gastric carcinoma in different countries (causing, for example, between one-half and two-thirds of all cancer deaths in Scandinavian and Central European countries, as against one-quarter of cancer deaths in Great Britain and Australia) are very probably the result of different culinary and dietetic habits.

While many of the earlier experimental attempts to produce alimentary carcinomas by giving carcinogenic hydrocarbons with food were unsuccessful, more recent work has shown that it is possible to produce both gastric and intestinal carcinomas in mice in this way. The gastric tumours obtained have all been squamous-cell tumours of the forestomach (Peacock and Kirby, 1944; Peacock, 1957; Stewart and Lorenz, 1949; Berenblum and Haran, 1955); but Lorenz and Stewart (1940) obtained adenocarcinomas of the small intestine by feeding with methylcholanthrene and dibenzanthracene. Further experiments with ingested carcinogens are needed; and the fate of the carcinogens in the alimentary tract, and whether they are present in the fæces, are subjects which require investigation. By intrarectal applications of methylcholanthrene, Berenblum, Haran and Rosin (1956) produced sarcomas, but no carcinomas, in mice.

Inhaled Carcinogens and Respiratory Cancers.

When mice are either skin-painted with carcinogens or given injections of them by any route, they show an increased incidence of the multiple adenomas of the lungs (Tyzzer's tumours) to which they are spontaneously liable. This result is of interest in reminding us not to overlook the possibility of such remote action in the causation of lung cancer; but, clearly, the direct effect of inhaled carcinogens is a more probable mode of action. Many inhalational experiments have been performed, by the use of soots, bituminous smokes, tobacco smoke, motor-exhaust gases, road dust, other siliceous and metallic dusts, radioactive dusts and finely-powdered carcinogenic hydrocarbons. An increased incidence of lung tumours, mainly Tyzzer adenomas, was obtained by Campbell (1940-1943) with dusts from tarred roads and with dusts containing silica and oxide of iron; but this result is of uncertain significance, as Tyzzer tumours are doubtfully comparable with human carcinomas (McDonald and Woodhouse, 1942).

With tobacco and other organic smokes, the results of a vast number of inhalation experiments have been disappointingly negative or equivocal, even when the smoke is known to contain hydrocarbons. Thus benzpyrene and many other polycyclic hydrocarbons are present in cigarette smoke (Cooper and Lindsay, 1955; Wynder and Wright, 1957; Wynder and Hoffman, 1959) and the smoke from stubs contains much more of these, including four times more benzpyrene, than the smoke from tips (Lindsay, 1959); yet prolonged exposure of mice to atmospheres containing cigarette smoke has failed to evoke any bronchial carcinomas. However, such inhalation experiments are in several ways unsatisfactory, and their negative results are of little significance. When smokes are puffed into cages, much of the material is quickly deposited, and most of that which is inhaled by the animals may well be arrested in, and expelled from, the nasal passages and may never reach the lungs. Moreover, the very substances in the smoke which are most under suspicion — namely, benzpyrene and other polycyclic hydrocarbons — are those which, as Kennaway and his co-workers first showed, are constituents of the higher boiling fractions of artificial tars; and for this reason they will be among the first components of the smoke to condense on the cage. The inhalation of cold dispersed smoke puffed into a cage is very different from the smoker's inhalation of nascent material direct from its burning source.

Experimental skin applications of condensates of cigarette smoke produce skin cancers (Wynder, 1959). This is not an unexpected result, since the material is known to contain at least benzpyrene; although certainly of some significance, it does not prove anything conclusive about lung carcinogenesis. What is needed is some technique which will bring the suspected material into close and prolonged contact with bronchial epithelium. Lasnitzki (1956 and 1958) used cultures of human fœtal lung and found that condensates of cigarette smoke produced epithelial hyperplasia and abnormal mitoses, similar to those produced by benzpyrene; but long-term experiments of this kind may not be practicable. Blacklock (1957) obtained one carcinoma in 18 rats receiving direct intrapulmonary injections of cigarette tar, and this method should be used on a larger scale. In collaboration with Dr. J. W. Cook of Exeter, and with the help of Dr. Hou Lee-Tsun, I am carrying out a series of experiments on the effects of various fractions of cigarette-smoke condensates on subcutaneous and intramuscular grafts of embryonic lung tissue in rats. This technique is similar to that used by Horning (1950), who obtained bronchial carcinomas from subcutaneous homografts of lung tissue contaminated with methylcholanthrene and other carcinogens.

It must be added here that tobacco smoke is not the only source of inhaled carcinogenic hydrocarbons. The soot of city air, the main source of anthracosis in city dwellers, contains benzpyrene and other polycyclic hydrocarbons (Waller, 1952), and these may account for the fact that lung cancer has a higher urban than rural incidence, as has been shown, for example by Stocks and Campbell (1955) and by Stocks (1959).

Sarcomas and Gliomas Produced by Carcinogenic Hydrocarbons.

Small quantities of carcinogenic hydrocarbons introduced directly into connective tissue readily evoke sarcomas in many species of animals, and when introduced into the brain they evoke gliomas. At first sight it would seem unlikely that these tumours, resulting from artificial injections of non-physiological substances into tissues to which they cannot gain access under natural circumstances, can have any human counterparts. But when we recall that the benzanthracene group of hydrocarbons, especially cholanthrene and methylcholanthrene, are chemically akin to the bile acids and sterols, we must concede the possibility that chemical changes of these normal substances, occurring in pathological tissues in traumatic, inflammatory or degenerative lesions, might produce carcinogens. However, this is purely speculative; and unfortunately, testing of the hypothesis is likely to be very difficult or impossible, since we know from experiments with known carcinogens that extremely minute quantities can evoke sarcomas, and since suitable extracts of some normal tissues and even highly purified cholesterol can induce

sarcomas in rats and mice (Kennaway, 1957; Hieger, 1959).

Remote Action of Carcinogenic Hydrocarbons.

The carcinogenic action of hydrocarbons is not restricted to the tissue to which they are locally applied. From their initial site of application they are absorbed and carried throughout the body by the circulation. Certain tissues, for example, adipose tissue and brain, retain them for a time, but they are soon metabolized, mainly in the liver, and they or their metabolites are excreted in the bile and the urine (Peacock, 1957). There have been many experimental results which have shown that carcinogens, after their absorption, may have a carcinogenic effect on remote tissues. Thus, after the administration of carcinogens by any route, mice often show an increased incidence of lung adenomas, lymphoid tumours or liver tumours; and Orr (1943) found many mammary carcinomas in mice which had been given methylcholanthrene intranasally. Whether or not any human tumours result from remote action of absorbed hydrocarbons we do not know; as far as I am aware, chimney-sweeps, cotton-spinners and tar and oil workers have not shown any disproportionate liability to tumours of any tissue except the directly contaminated skin.

Hepatic Carcinogens.

Since the discovery in the early 1930's that certain azo-dyes were potent and selective hepatic carcinogens for rodents, many other substances have been found experimentally to be carcinogenic for the liver. These include dibenzarbazole (Cook *et alii*, 1937), acetylaminofluorene (Wilson *et alii*, 1941; Bielschowsky, 1944), dimethylnitrosamine (Magee and Barnes, 1956; Christie, 1960, unpublished), thioacetamide (Gupta, 1956), 4'-fluoro-4-aminodiphenyl (Matthews and Walpole, 1958) and the pyrrolizidine alkaloids of *Senecio* and some other plants (Barnes and Schoental, 1958); and even carbon tetrachloride may evoke hepatomas in mice (Edwards, 1941). None of these substances is known to have caused hepatic cancer in man. But on general grounds, it is very probable that unidentified toxic agents are responsible for much of the hepatic cirrhosis and cancer, the causes of which are still unknown; and Barnes and Schoental have suggested the possibility that alkaloids of *Senecio* and other plants may play a part in the causation of the very prevalent liver cancers of the Bantu and other African races. All experimentally proved hepatic carcinogens must be held under suspicion as possible factors in man, and they and kindred substances must be diligently searched for in the environment of patients with liver tumours.

Urinary Carcinogens.

Bladder, Ureter and Renal Pelvis.

It was the occupational incidence of so-called "aniline" cancer of the bladder in man that led to the experimental identification of beta-naphthylamine as a potent and selective urinary-tract carcinogen (Hueper *et alii*, 1938; Bonser, 1943). Bonser *et alii* (1951 and 1958) then showed that excreted derivatives of beta-naphthylamine were the effective agents. More recently, benzidine and 4-aminodiphenyl have also been incriminated as both occupational and experimental urinary-tract carcinogens (Walpole and Williams, 1958). Other substances which have been found to produce urinary-tract tumours experimentally, although they are not known to produce human tumours, include azo-dyes, acetylaminofluorene and several ortho-aminophenols. The last are of special interest, as some of them are metabolites of tryptophane and are known to be present in human urine (Boyland, 1958). The causes of most urinary-tract tumours in man are still unknown; but in the light of the experimental findings, it is very probable that the causes of most of them will be found amongst the many dyes, preservatives and other additives in confectionery, cordials, foods and cosmetics, as well as amongst the reagents used in industry.

The Kidney.

In view of the excretory functions of the kidney, it is rather surprising that no occupational or other chemical factor has ever been incriminated, or even suspected, as a cause of carcinoma of the human renal parenchyma, and that very few chemical agents have been found experimentally to be renal carcinogens. Sempronj and Morelli (1939) obtained adenocarcinoma of the renal parenchyma in rats which had received subcutaneous injections of beta-anthraquinoline, a result which, as far as I know, has not been repeated; Bielschowsky and Green (1945) saw anaplastic renal carcinoma in a single fowl which had been treated with acetylaminofluorene; and Magee and Barnes (1959) reported renal adenocarcinomas in rats treated with dimethylnitrosamine. This last research is, I think, of special interest; Magee and Barnes, who are about to publish a fuller account of it, have shown me specimens of the large numbers of tumours they have obtained, and the structure of these closely resembles that of human renal carcinomas, ranging from well-differentiated tubular adenocarcinomas, some of clear-cell type, to highly anaplastic growths, the epithelial nature of which is difficult to recognize — just as occurs with human tumours. The development of renal adenocarcinomas in hamsters after prolonged œstrogen administration (Kirkman and Bacon, 1952; Horning and Whittick, 1954; Horning, 1956) is a very peculiar and unexpected result, and calls for further investigation.

Metallic Elements and Salts, and Plastic Films.

Before the discovery of pure carcinogens and when "chronic irritation" was regarded as an important cause of cancer, many experiments were carried out with ordinary inorganic acids, alkalis and salts in an attempt to induce tumours. Most of these were unsuccessful, and the occasional positive results were of doubtful significance. The only human cancer attributable to an inorganic agent was carcinoma of the skin supervening on chronic arsenical dermatitis; and repeated attempts to produce arsenical cancer experimentally gave only occasional positive results. The more recent experimental production of sarcomas by means of powdered cobalt (Heath, 1956) or nickel (Hueper, 1958) or iron-dextran complex (Richmond, 1959) has not, as far as I know, been reduplicated in man; and the ready production of multiple sarcomas of bone in rabbits by means of beryllium salts (Barnes, Denz and Sissons, 1950; Dutra and Largent, 1950) has no known human counterpart. The discovery that bakelite discs, "Cellophane" or other plastic films, or metal foils, especially silver, embedded in the tissues of rats or mice may evoke sarcomas (Oppenheimer *et alii*, 1956 and 1958) is notable. Again, as far as I know, no cases of sarcoma arising around metal nails, sutures or filigrees or around silk or synthetic sutures in man have been reported.

Experimental Tumours of Endocrine Glands and of Endocrine Target Organs.

An enormous literature exists on this subject, and many different kinds of tumours have been induced by various methods involving hormonal disturbances. These include tumours of most of the ductless glands themselves — thyroid, pituitary and adrenal cortical tumours, granulosa-cell and other tumours of the ovaries and interstitial-cell tumours of the testis; but as far as I know, no parathyroid tumours, chromaffin tumours or tumours of the islets of Langerhans have been produced experimentally. The principal endocrine target organs, the tumours of which have been closely studied experimentally, are the breast and the uterus, and the experimental findings are of the greatest interest for human pathology. I will say no more of this subject here, except to refer you to the valuable reviews of Burrows and Horning (1952), of Shimkin (1957) and of Bielschowsky and Horning (1958), and to those in Volume 12 of the *Ciba Foundation Colloquia on Endocrinology* (1958).

Radiations as Carcinogenic Agents.

Light and Ultra-Violet Light.

It is now generally recognized that excessive exposure to sunlight is one of the most important causes of human skin and lip cancers. The skin tumours produced in rats and mice, especially albino animals, by exposure to sunlight or ultra-violet light (first by Findlay in 1928 and 1930, and later by many others) are clearly the exact counterparts of the human tumours, even to showing a similar diversity of structure, including both squamous-cell and basal-cell growths.

X Rays.

The well known squamous-cell carcinomas of the skin supervening on X-ray dermatitis in man, the occasional development of soft-tissue sarcomas in persons exposed to X rays, sarcomas of human bone resulting from previous X-ray treatment of other diseases, recently reported in increasing numbers (Sabanas *et alii*, 1956; Carrol *et alii*, 1956; Cruz *et alii*, 1957), cases of post-irradiational carcinoma of the thyroid gland (Wilson *et alii*, 1958; Goolden, 1958; Doniach, 1958) and post-irradiational leukæmia developing in people who have been subjected to X-ray treatment for spondylitis (Court-Brown, 1958) — all these have been paralleled experimentally (Glucksman *et alii*, 1957).

Radioactive Substances.

Again, the occasional carcinoma of the skin or sarcoma of deeper tissues which has developed in man after radium applications, and the well-known multiple sarcomas of the bones which developed in the painters of luminous watch dials in New Jersey, have been reduplicated experimentally. It is of great interest that the carcinogenic properties of "Thorotrast" (thorium dioxide), used in radio-diagnosis, were first demonstrated experimentally (Foulds, 1939) and that the human counterparts of the experimental tumours began to appear many years later. These have been angiosarcomas of the liver (MacMahon *et alii*, 1947; Tesluk and Nordin, 1955; Horta, 1956) and hepatic carcinomas (Roberts and Carlson, 1956; Morgan *et alii*, 1958; Gardner and Ogilvie, 1959).

Virus-Induced Tumours.

In Birds.

The Rous sarcoma and other filterable tumours of birds have been intensively studied for half a century; but whether or not they are properly comparable with mammalian tumours is still debatable. Three facts suggest that they may be a quite peculiar class of lesions *sui generis* — namely: (*a*) the filterable avian agents differ from other carcinogens in that they induce only the same kinds of tumours as those from which they came; (*b*) these agents are demonstrable only in certain tumours of mesenchymal tissues and never in epithelial tumours; and (*c*) sarcomas induced in fowls and other birds by chemical carcinogens do not contain filterable agents.

In Mammals.

The following four kinds of tumour-inducing viruses are known in mammals.

The "Milk Factor" in Mice.—This agent, transferred to the young in the mother's milk, is an important factor in the genesis of mammary cancer in many inbred strains of mice, but it is not present, at least demonstrably, in all mammary cancers in mice. Chemically-induced mammary cancer in low-cancer strains are devoid of it (Dmochowski and Orr, 1949), and there is no evidence of a "milk-factor" in other species or in man.

The Shope Tumour of Rabbits.—The filterable agent, present in the papillomatous lesions, is not demonstrable in the tissue of the cancerous growths which may supervene; but it is still uncertain whether this is because the virus is absent from the carcinomas or present in a masked or inactive form.

Filterable Mouse Leukæmias.—The recent discovery by Gross and others (Gross, 1958) that some mouse leukæmias are transmissible by cell-free filtrates is of great interest, but its significance for the ætiology of leukæmia in general remains to be assessed. In particular, we may ask what proportion of cases of spontaneous leukæmia in mice not belonging to the stocks in virus-infected laboratories can be shown to be virus-induced. There is a risk, when a striking discovery of this kind is first made, that the whole of the experimentalists' interest will be concentrated on the breeding and study of those particular animals which exemplify it, to the exclusion of those that do not.

Polyoma Virus.—This is a recently-discovered filterable agent recoverable from the tissues of some leukæmic mice and capable of evoking a great variety of tumours in the tissues of young mice, rats and hamsters (Gross, 1958; Negroni *et alii*, 1959). Further studies of this remarkable discovery will be awaited with great interest; it is too soon yet to see it in its proper perspective in the whole field of tumour causation.

The Electron Microscope.—In future research on virus-induced tumours the electron microscope will be an increasingly important tool (Dmochowski, 1957 and 1959). It is not too much to hope that, with increasing knowledge of the electron microscopy of normal and pathological tissues, this instrument may afford criteria for distinguishing between tumours caused by viruses and those not so caused, and that we shall be able to use these criteria to decide whether or not any human tumours are virus-induced. So far there is no real evidence that they are.

Concluding Comments.

I wish to end this brief survey with the following general comments.

1. Great advances in our knowledge of tumour causation have been made in the last three decades, refuting the idea, often implied and sometimes openly stated, that cancer research has been unproductive. It is only 30 years since Kennaway and his helpers first isolated a pure chemical carcinogen; since then, many hundreds of carcinogenic agents have been identified, and their number is constantly being added to. While, naturally enough, in the past the identification of carcinogens has often arisen directly out of our recognition of the occupational or habitual incidence of a particular kind of tumour, in future we may anticipate that substances which are first shown by experimental tests to be carcinogenic will later be recognized as factors in the causation of human tumours. Thus it may well be that the experimental incrimination of azo dyes or *Senecio* alkaloids as hepatic carcinogens, or of dimethylnitrosamine as a renal carcinogen, may lead to the detection of some of the hitherto unknown causes of hepatic and renal tumours in man. All experimentally identified carcinogens are therefore worthy of careful study.

2. It is surely an encouraging fact that for one important tissue, the skin, the external causes of the great majority of cancers have been identified. There are now relatively few cutaneous carcinomas that cannot be attributed to the effects of known chemical agents, light or ionizing rays. Naturally enough, our knowledge of the causation of most visceral cancers is far less certain and complete; but many promising lines of thought and experimental study have already been plotted; and there is every reason to believe that increasing knowledge of ingested and inhaled carcinogens and of endocrine physiology will eventually lead to the effective control of our commonest visceral cancers, those of the alimentary canal, the lungs, the breast and the uterus.

3. It is important to recognize that human tumour causation is much more complex than its experimental

counterpart. In the controlled experiment, we usually use test animals of standard, often homogeneous inbred, stock; and we usually apply a single carcinogenic agent at regular intervals and in known dosages. In the human experiment which Nature performs, the test animals are genetically very heterogeneous, and the carcinogens that are applied to them are often multiple in kind and irregular in dosage and times of application. A skin cancer in man must be thought of as being often the result of the summative effects of several different chemical agents, and sometimes of light or other physical agents also, acting either simultaneously or successively, their action often being accelerated or retarded by the effects of various co-carcinogens or anticarcinogens. Many visceral cancers are probably of even more complex causation, and the elucidation of their causes will be correspondingly more difficult.

4. Finally, we must constantly bear in mind the fact that chemical carcinogens, comparable with some of those already known, may be formed endogenously in the body itself under pathological conditions. This might occur, for example, in the contents of the obstructed mammary ducts in precancerous cystic hyperplasia of the breast, in the gall-stones which commonly precede cancer of the gall-bladder, in the sebaceous contents of the ovarian dermoid cyst that suffers cancerous change or in the retained smegma of the cancerous penis. Indeed, as regard smegma, this idea has been experimentally established; both human smegma and horse smegma have been shown to be feebly carcinogenic. The search for chemical carcinogens in precancerous lesions will be an important task in future cancer research.

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HÆMOLYTIC DISEASE OF THE NEW-BORN.[1]

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HÆMOLYTIC DISEASE of the new-born, since successful treatment with replacement transfusion has become available, has assumed great importance in the management of the new-born. In all except a few cases, proper treatment can save a life or prevent permanent crippling brain damage.

Hæmolytic disease due to Rh incompatibility in a white population occurs in one out of 150 to 200 full-term pregnancies (Levine, 1948). Roughly, 13% of marriages are between an Rh-positive man and an Rh-negative woman, and in this group full-term infants will be affected to some degree in one in 20 to one in 26 pregnancies (Levine, Vogel and Rosenfield, 1953).

Management commences with the diagnosis of pregnancy, when the mother's Rh group must be determined. Should she be Rh-negative, inquiry should be made as to whether she has been pregnant before, or whether she has received a transfusion or an injection of blood at any time in her life. If one can be reasonably certain that the answer to both these inquiries is negative, for all practical purposes an affected infant will not result from this pregnancy. If the answer is affirmative, the next step is to determine the Rh group of the husband. If he proves to be Rh-negative, no further anxiety need be felt, but if he is Rh-positive, one should assume that the infant at birth may be affected by hæmolytic disease of the new-born.

It has been customary, when Rh incompatibility has been found between husband and wife and there has been a previous pregnancy or other source of immunization, to seek maternal antibodies to D during pregnancy. The maternal serum has been examined for antibodies by the indirect Coombs test before the end of the fourth month. If antibodies are found, the antibody titre is estimated and again at about the thirty-second week. It should be emphasized that these antibody titres are highly unreliable, and a rise in titre or a high titre does not mean that an affected infant will be born; conversely the absence of agglutinins does not mean than an unaffected infant will be delivered. Such antibody titres have been a source of great error on many occasions, either lulling the attending practitioner into a feeling of false security, or causing the unnecessary transport over a long distance of an infant who does not need any treatment.

Kirk, Vos and Kelsall (1958) claim to be able to predetermine the severity of the disease in the infant prior to delivery by means of the indirect Coombs titration of maternal antibody, but their work has not been confirmed. The only safe rule is to regard all second and subsequent infants of Rh incompatible marriages as being possibly affected and possibly requiring a replacement transfusion.

This raises the question as to where the Rh-negative mother, who may have an affected infant, should be delivered. It has been advocated that all such mothers should be delivered in the large metropolitan hospitals, who have the pædiatric and pathological services for managing the infant (Bourke, 1955). In this country this is considered impossible on several grounds. In New South Wales, in 1958, 75,370 infants were delivered. Of these, 51,018 resulted from second or subsequent pregnancies (Cuthbert-Browne, 1960). Thirteen *per centum* of these, or 6630, would result from Rh incompatible matings, and theoretically this number of infants could be affected and require treatment. Even if it was possible for this number to be accommodated in the large metropolitan hospitals, it is extremely doubtful whether one

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 29, 1960.

could persuade country mothers to separate themselves from their families for a month before their due date of confinement, to stay in the city and to be confined in alien surroundings amongst strangers, even if they could afford the financial outlay this would entail.

The vast majority of infants affected by hæmolytic disease of the new-born are born in good condition, and treatment by replacement transfusion is not a matter of a few hours. They travel quite well by air and except in extremely hot weather, by road transport. It would seem more practical to transport these infants, if affected, to a centre where there is the pædiatric and pathological experience to manage them. Those severely affected or of low birth weight should travel in an incubator; or a pædiatrician and, in some cases, a pathology technician could travel to the country hospital and manage the infant. Actual delivery in a metropolitan hospital is obligatory when a previous infant has died of hæmolytic disease of the new-born or has been very severely affected. When there has been a significant rise in antibody titre in the maternal serum between the sixteenth and thirty-second weeks and when the necessary services are not available reasonably close, arrangements for delivery in the metropolitan area should be made.

When there is reasonable evidence that an affected infant will be born, the question of premature induction of labour arises. The management of infants with hæmolytic disease of the new-born is much more difficult if they are premature and of low birth weight. When there is no history of a severely affected infant being born previously, pregnancy should be allowed to go to full term. It may be advisable, with mothers from isolated areas who have a significant rise in antibody titre during pregnancy, to bring them to the metropolitan area during the thirty-seventh week and induce labour during the thirty-eighth week if the infant in the uterus seems of reasonable size. When a previously severely affected infant has been born within two weeks of full term, who has survived with several replacement transfusions, or who would probably have survived if so treated, induction of labour is indicated in a subsequent pregnancy between the thirty-sixth and thirty eighth weeks.

The most difficult problem arises when there is a history of one or more previous infants stillborn because of undisputed hydrops fœtalis. Infants so severely affected must be delivered before their disease has progressed to hydrops fœtalis of any degree, because, once this has occurred, it is almost impossible to keep them alive. This means that delivery may be necessary as early as between the thirty-second and thirty-fourth weeks of pregnancy. Admittedly, the chance of survival at this gestational age is slight; but once hydrops fœtalis has developed, it is almost nil.

When such a problem arises, one must try to determine whether the husband is homozygous or heterozygous Rh-positive. With various antisera one can estimate the chances of his being homozygous or heterozygous, but in the absence of anti-d serum, one can never be certain. However, if one of his parents or one of his previous children is Rh-negative, one can safely say that he is heterozygous and one can then have an even chance of the infant's being Rh-negative and unaffected. Unfortunately, one or both of the husband's parents are often dead, and often his only surviving child is that from the first pregnancy of his Rh-negative wife. Artificial insemination from an Rh-negative donor is one answer, but a most unsatisfactory one in almost all cases.

Some help can be obtained in this problem by examination of the amniotic fluid (Cary, 1960). A sample of amniotic fluid is obtained by puncturing the uterus through the abdominal wall at weekly intervals, beginning at the thirtieth week. This fluid is then examined spectrophotometrically for bilirubin. A curve is produced which indicates whether the infant is affected or not, and when it is so affected, that it has to be delivered to have a chance of survival.

When an infant is expected that is reasonably likely to be affected and to need treatment, three people are concerned — the obstetrician, the pathologist and the pædiatrician. All three are essential, and all must work together. As soon as the mother goes into labour, 800 ml. of group O, Rh-negative blood should be obtained. This is cross-matched with the mother's serum, and if compatible will be suitable for use in replacement transfusions of the infant. Rh-positive blood has been used (Stening, 1956) for replacement transfusion, with the idea that it will absorb circulating agglutinin; but this does not sem to confer any advantage. Citrated blood which has been collected not more than four days previously is usually used. Recently collected heparinized blood is preferable, if it can be obtained, as the infant does not then have to handle the large amount of citrate in citrated blood. The bottles of blood should be shaken as little as possible, so that the red cells can settle to the bottom. While labour is in progress, preparations are made to carry out replacement transfusion should this be necessary, or transport is arranged so that the infant can be sent to a centre for this procedure.

As soon as the infant is born, the umbilical cord is clamped about two inches from the skin and the cord is cut. The maternal end of the cord, while still pulsating, is allowed to bleed into two specimen tubes. One tube contains anticoagulant such as dried oxalate or a drop of heparin solution, but not citrate solution, which may dilute the specimen so that the subsequent hæmoglobin value will be falsely low. One person must be responsible for seeing that the anticoagulant is properly mixed with the collected blood. This specimen must not be allowed to clot. One specimen having been collected into anticoagulant, another tube is filled with blood and allowed to clot to obtain serum.

When these specimens have been collected, the infant is examined. Yellow vernix always means a severely affected infant, as does a large, thin placenta. Such an infant is usually limp, pale and slow to breathe, and has a weak, moaning cry and a grossly enlarged liver and spleen. Despite a high level of bilirubin in the blood, jaundice is never present at birth. It may appear very rapidly, but exposure to light seems to be necessary and for this reason is first noticed and becomes most marked on the face. Subcutaneous bruising also appears rapidly in such severe cases. In very severe cases there may be a varying degree of generalized œdema with ascites and hydrothorax. If such œdema is marked, the infant does not breathe, or if it does, death occurs in periods varying from a few minutes to several hours.

As a rule the average infant establishes respiration normally, has good muscle tone, cries lustily, has a normal skin colour and, apart from slight enlargement of the spleen, appears perfectly normal.

Once the examination has been completed, the cord is tied just proximal to the clamp, which is removed. No dressing is applied, and the infant is weighed and measured, wrapped in a sterile blanket and placed in a cot or warmed incubator if available. Oxygen is given if respirations are not normal. Patent metallic clamps must not be applied closer than two inches from the skin. Such clamps are usually placed close to the skin, and when removed leave only a minute piece of cord, which makes impossible more than one use of the umbilical vein for replacement transfusion.

A practical point now arises as to whether the pathologist should be asked to examine the cord blood immediately in all cases when there is Rh incompatibility, if the infant has been born late at night or in the early hours of the morning. The blood should be examined immediately if there has been an affected infant from a previous pregnancy, if there has been a rise in antibody titre during this pregnancy, if there is pallor, bruising, splenomegaly, yellow vernix or œdema, if the infant is premature or if the birth weight is below 6 lb. If none of these abnormalities is present, examination of the cord blood can be deferred to a more

convenient time, but not longer than 10 hours. It is emphasized that the cord blood should be collected from all second and subsequent infants when the parents are Rh incompatible. If there is gross disease with œdema and the infant is distressed, replacement transfusion should be started as soon as possible without waiting for confirmatory pathological tests.

The purpose of examining the cord blood is twofold. It has to be decided whether the infant has hæmolytic disease of the new-born and, if so, whether replacement transfusion is going the be necessary. The first decision rests largely on the result of the direct Coombs test on the infant's blood. This is an easily performed test, and if the result is positive, indicates that the red cells are coated with antibody and that the infant has hæmolytic disease of the new-born due to Rh incompatibility. However, in inexperienced hands false negative results are not uncommon, especially when the coating with antibody is slight. A useful confirmatory test is to determine the Rh group of the infant. If the infant is Rh-positive and there is definite clinical evidence of hæmolysis, it is best to assume that a negative response to the direct Coombs test is wrong and to proceed as if the test had given a positive result. Another possible source of confusion is that an Rh-positive infant whose cells are heavily coated with antibody may react as Rh-negative. Such infants give a positive response to the direct Coombs test and have obvious evidence of disease. If the result of the direct Coombs test is negative and the infant is Rh-negative, is of normal colour and exhibits no splenomegaly, one can assume that hæmolytic disease of the new-born due to Rh incompatibility is not present.

However, if from examination of the cord blood one has decided that hæmolytic disease of the new-born is present, one must then determine whether replacement transfusion is indicated. There is no doubt that removal of a large amount of the infant's Rh-positive red cells coated with antibody and their replacement by a donor's Rh-negative cells as early as possible will prevent severe jaundice in the vast majority of cases. However, it should also be remembered that replacement transfusion may be difficult and may cause the infant's death, so it should not be carried out unless it is necessary.

The hæmoglobin value in grammes per 100 ml. is the most commonly considered index. The level below which replacement is indicated has varied with different authorities. Diamond and Allen (1952) stated 15 grammes per 100 ml., Mollison and Cutbush (1951) 14·5 grammes per 100 ml., Mollison, Mourant and Race (1952) 15·5 grammes per 100 ml. and Polacek (1955) 12 grammes per 100 ml. From 1952 to 1958 I considered that at a level below 15 grammes per 100 ml. a replacement transfusion was indicated for an affected infant. During 1959, several infants with cord hæmoglobin levels between 13 and 15 grammes per 100 ml. for various reasons did not receive immediate replacement transfusions, and did not subsequently develop jaundice of any severity.

At St. Margaret's Hospital for Women, the cord blood of all Rh-negative multiparous mothers with Rh-positive husbands is collected as a routine measure, and a direct Coombs test, Rh grouping and estimation of the hæmoglobin value are carried out. A consecutive series of 100 Rh-negative infants from such parents who were therefore unaffected was obtained. These infants had cord hæmoglobin levels varying from 12·5 to 20·7 grammes per 100 ml., with a mean of 16·8 grammes per 100 ml. Twelve infants had a cord hæmoglobin value of less than 15 grammes per 100 ml. (Figure I). It would seem, therefore, with the method used at this hospital at least, that all affected infants with cord hæmoglobin levels between 12·5 and 15 grammes per 100 ml. do not necessarily have to have an immediate replacement transfusion. It is considered that if an affected infant has a hæmoglobin level in the cord blood of less than 13 grammes per 100 ml., replacement transfusion is indicated, but if the hæmoglobin level is above this, further evidence is necessary.

The serum bilirubin level in the cord blood is a valuable guide, despite the well-known statement that the combination of hæmoglobin and bilirubin levels gives no better guide than the hæmoglobin level alone (Mollison and Cutbush, 1949). Low values are of little help; but if the cord serum bilirubin level is above 4 mg. per 100 ml. and there is also a cord hæmoglobin level below 15 grammes per 100 ml., replacement transfusion is indicated.

It is considered that in an infant of a known Rh incompatible mating, the direct Coombs test, the Rh grouping, the hæmoglobin levels and in some cases the serum bilirubin level, will, in combination, indicate whether a replacement transfusion as soon as possible is necessary.

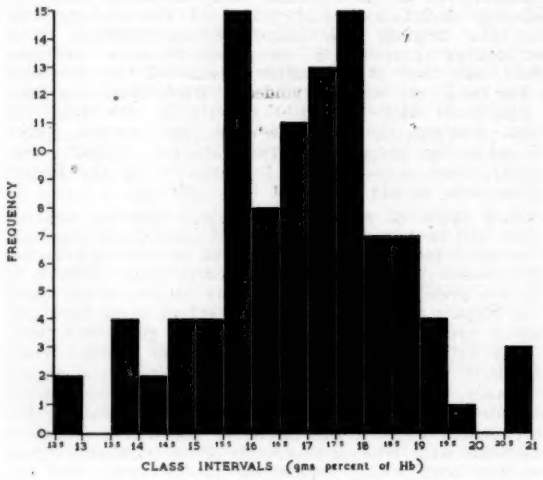

FIGURE I.
Frequency distribution: hæmoglobin value of 100 Rh-negative cord blood samples.

Two other examinations of the cord blood have been used — the reticulocyte level expressed as a percentage of red cells and the nucleated red-cell level expressed as a percentage of the nucleated blood cells. It was thought that a reticulocyte figure of more than 10% or a nucleated red-cell figure of more than 20% in an affected infant indicated a replacement transfusion. In practice it is found that in the severely affected infant these figures will be much higher. In the infant who may or may not require a replacement transfusion, they are of little value in prognosis.

The decision as to whether replacement transfusion should be carried out as soon as possible may be influenced by the birth weight of the infant and its state of maturity. An affected infant of less than 5 lb. 8 oz. birth weight or of gestational age less than 37 weeks will need a replacement transfusion almost invariably, and the sooner it is done, the better. A previous infant born with the disease should not influence the decision. If a previous infant has been severely affected, a subsequent affected infant will show evidence of severe disease on clinical examination or in its cord blood. One should remember that a previous infant who has had a replacement transfusion may have been premature and of low birth weight, or even the replacement transfusion may not have been necessary. Similarly, a history of a previous stillbirth may not indicate that the mother is highly sensitized, as the previous intrauterine death may not have been due to hæmolytic disease of the new-born.

To summarize: a replacement transfusion as soon as possible is indicated for (i) an infant with severe signs of the disease at birth, (ii) an affected infant with a low birth weight or a premature infant, (iii) an affected infant with a cord hæmoglobin level of less than 13 grammes per 100 ml. or (iv) an affected infant with a cord hæmoglobin level of less than 15 grammes per 100 ml. and a cord bilirubin level of greater than 4 mg. per 100 ml.

Should it be judged that an affected infant does not require replacement transfusion as soon as possible, what further should be done? First, it must be emphasized that the cord must be kept as dry as possible, so that it will not separate. The best way of doing this is to keep the infant in a closed incubator and have no dressing on at all. If no incubator is available, the cord should be covered with two layers of thin gauze, and this dressing should not be disturbed. Overclothing in hot weather, with sweating and consequent maceration of the cord, should be avoided. Normal breast feeding is carried out, but above all, the infant should not be bathed. The appearance of jaundice should be carefully watched for. It will first appear on the exposed skin — that is, the face — but cannot be considered to be very significant unless it can be detected on the covered skin — that is, the abdomen or legs — after blood has been expressed from the skin by pressure. Jaundice can be accurately assessed only in daylight. The age at which definite jaundice appears is important. If it appears within 12 hours, replacement transfusion is indicated. If it appears within 24 hours, replacement transfusion will probably, but not invariably, be necessary. Occasionally an affected infant will not appear jaundiced in the first 24 hours, but jaundice appears in the second 24 hours and rapidly increases. Estimations of the serum bilirubin level in the capillary blood should be carried out to decide whether replacement transfusion is indicated.

If any hospital is going to manage hæmolytic disease of the new-born, it must have available a pathologist who can estimate the bilirubin levels in capillary blood. Collection of sufficient blood from a cut in the heel is not easy and special apparatus is necessary to make these estimations on small amounts of serum.

At this point it is necessary to mention some modern views on bilirubin which are of the greatest importance in the management of hæmolytic disease of the new-born. When the hæmoglobin of red blood cells is broken down, the yellow pigment bilirubin is formed, which is insoluble in water, but soluble in alcohol — the so-called indirect-reacting bilirubin of van den Bergh. This bilirubin then passes through the liver cells, where it is linked with glucuronic acid to form conjugated bilirubin, which is water-soluble — the so-called direct-reacting bilirubin (Cole and Lathe, 1953). The non-conjugated indirect-reacting bilirubin is concerned with the damage to the basal nuclei in the brain, whereas the conjugated direct-acting bilirubin is not. However, both pigments will produce a yellow colour in the skin. It is, therefore, of the greatest importance for the pathologist to be able to determine the levels of both non-conjugated and conjugated bilirubin in the serum, because it is only on the level of the former that the decision to carry out replacement transfusion is made. A suitable method of estimation of non-conjugated and conjugated bilirubin levels is described by King and Wootton (1956).

It is very necessary to realize that the main purpose in the treatment of hæmolytic disease of the new-born is to prevent nuclear damage, which is associated with high levels of non-conjugated bilirubin the the blood. The infant at birth is unable to conjugate bilirubin to the water soluble bilirubin glucuronide, owing to the absence of glucuronyl acid transferase in the liver, and until it is able to do this, bilirubin cannot be excreted. The whole purpose of replacement transfusion is to remove non-conjugated bilirubin from the blood, so that a level is not reached at which nuclear damage will occur. This reduction of the non-conjugated bilirubin level must be continued until the glucuronyl acid transferase system is fully developed on about the fourth or fifth day of life, and the infant can adequately excrete its bilirubin in a water-soluble form.

The whole problem of treatment is related to early jaundice, and if jaundice appears early, the infant is in danger and may need treatment. If examination of the cord blood has not indicated that immediate replacement transfusion is necessary and jaundice subsequently appears, laboratory estimations of the serum non-conjugated bilirubin level are necessary, repeated until the level has begun to fall. Similarly, if any infant, whatever the blood group of the parents, develops definite jaundice in the first 24 hours of life, it almost invariably has hæmolytic disease of the new-born in some form and needs estimation of the non-conjugated bilirubin level in its serum. If this jaundice appears within 12 hours of delivery, almost invariably replacement transfusion will be necessary, and such infants should be regarded as presenting medical emergencies.

At what serum bilirubin level should replacement transfusion be carried out? I have never seen kernicterus develop in a mature infant with a bilirubin level of less than 30 mg. per 100 ml., but it is not suggested that replacement transfusion should be deferred until this level has been reached. A level of 20 mg. per 100 ml. was recommended by Diamond and Allen (1952) and by Levine, Vogel and Rosenfield (1953), and a level of 25 mg. per 100 ml. by Gaffney (1954). It should be realized that these were the levels of total bilirubin, as at these times the differentiation of non-conjugated and conjugated bilirubin was not considered important. Until 1960 I carried out replacement transfusions if the total serum bilirubin level was rising at a rate greater than 1 mg. per 100 ml. per hour, or if it exceeded 20 mg. per 100 ml. in the first 96 hours of life. This has been found safe and kernicterus has never occurred when this rule was followed. However, it is very probable that many replacement transfusions on patients with total serum bilirubin levels of 20 mg. per 100 ml. or more will be unnecessary, especially on the third and fourth days of life, as by this time a considerable proportion of the total serum bilirubin will consist of the conjugated fraction which is not related to kernicterus. It has always been a puzzle why certain infants have not developed kernicterus despite very high total serum bilirubin levels and this has been ascribed to varying amounts of constitutional susceptibility. It is very probable that the non-development of kernicterus with these very high levels was due to the fact that a high proportion of the total bilirubin was in the conjugated form.

It is now thought that replacement transfusion is indicated only after birth when the level of non-conjugated bilirubin exceeds 20 mg. per 100 ml. in the first 96 hours of life in a mature infant. This level is only tentative at present, and may be modified later, as it has been followed in only 15 patients, none of whom have shown any evidence of kernicterus. This level of 20 mg. per 100 ml. of non-conjugated bilirubin also indicates the performance of a repeat replacement transfusion.

The estimation of the capillary hæmoglobin level is of no value in estimating the amount of hæmolysis that has occurred. Study of Figure II will show numerous examples of infants with high serum bilirubin levels who have high hæmoglobin levels. Many of these infants were in grave danger of developing kernicterus, but one would not suspect the height of the serum bilirubin level from estimating the hæmoglobin level. The reason for these paradoxically high hæmoglobin levels is obscure, but possibly entry of stored red cells into the circulation plays a part.

Estimations of the reticulocyte or nucleated red cell levels have not been helpful in deciding whether a delayed or repeated replacement transfusion should be carried out.

Confusion may arise when jaundice appears early in an infant whose mother is Rh-positive. As was mentioned earlier, jaundice in the first 24 hours of life must be regarded as due to hæmolytic disease of the new-born. The incompatibility between mother and infant may be due to one of the rarer types of sensitization, the commonest being c and E. The sensitization as a rule is mild, but the infant may need replacement transfusion. Sensitization has been reported to the Kell and Duffy antigens (Simmons, 1956; Barker *et alii*, 1956). The red cells of these infants react positively to the direct Coombs test.

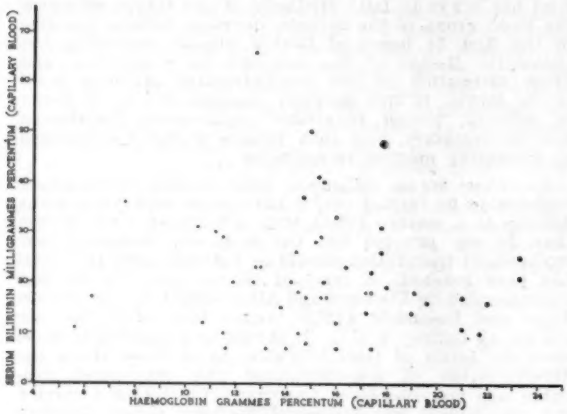

FIGURE II.

The commonest cause of hæmolytic disease of the new-born with jaundice in the infants of Rh-positive mothers is A B O incompatibility. The mother's blood is group O and the infant's usually group A, although the latter may be group B or AB. The mother's group O blood contains naturally occurring antibodies to A and/or B red cells, so that the first-born infant is often affected. Jaundice as a rule is not severe and does not occur as early as in Rh incompatibility; but I have seen three babies with kernicterus, one of whom died. The infant's blood rarely reacts positively to the direct Coombs test, but in a stained film many microspherocytes will be seen. The fragility of the infant's red cells is increased.

Although the cause of sensitization is unknown, the early appearance of increasing jaundice indicates danger. Jaundice in the first 48 hours of life means that replacement transfusion will be necessary if the non-conjugated bilirubin level rises at a rate of more than 1 mg. per 100 ml. per hour, or exceeds a level of 20 mg. per 100 ml. at any time. Infants with A B O incompatibility often do not conjugate bilirubin for 7 to 10 days and replacement transfusion may be necessary much later than where the infant is affected by rhesus antibodies.

Jaundice of prematurity requires separate consideration. Many premature infants become jaundiced, some severely. In the absence of Rh or A B O incompatibility, this jaundice is noticeable about the third day of life, and may continue to increase to about the sixth or seventh day. The jaundice of prematurity is probably due to delayed functioning of the glucuronic acid transferase system. This leads to delay in conjugation of bilirubin formed from normal breakdown of excess hæmoglobin present at birth, with delay in its excretion. Jaundice therefore increases, and kernicterus may occur as late as the ninth day, whereas it is extremely unlikely to occur after the fourth day in the mature infant. Replacement transfusion is difficult, because of the small size and immaturity and because the umbilical cord has usually separated, making a "cut down" on a large vein necessary. However, replacement transfusion must be done if the level of non-conjugated bilirubin exceeds 20 mg. per 100 ml. and probably at lower levels if the infant weighs less than 3 lb. or there is any evidence of cerebral anoxia at birth.

The clinical picture of kernicterus in the mature infant is sufficiently characteristic to be diagnosed or excluded in the neonatal period. I have not seen it before the third day and only once after the fourth. An infant who, apart from jaundice, has been normal, will refuse to feed and may vomit. The infant is lethargic, the Moro reflex previously present disappears. After a few hours pathognomonic signs appear. These are extension of the arms and wrists with inward rotation, extension of the legs, and a position of opisthotonus with retraction of the head and arching of the back. These may result from stimulation, but later become persistent. The other important signs are transverse furrowing of the forehead and conjugate downward deviation of the eyes producing a "setting sun" appearance, with a semicircle of white sclera between the iris and the upper lids. Convulsions are rare in my experience and usually indicate coexistent cerebral hæmorrhage. Death, if it occurs, is preceded by irregular respirations, moist sounds in the chest and the appearance of a blood-stained nasal discharge.

The premature infant with kernicterus following jaundice of prematurity will usually show a similar clinical picture. However, kernicterus may cause only lethargy, poor sucking and absence of the Moro reflex. The full picture of opisthotonus, extension of the limbs and conjugate downward deviation of the eyes may be seen on response to stimulation only after some weeks.

Many infants with milder degrees of hæmolytic disease of the new-born do not become sufficiently jaundiced to require replacement transfusion. However, their red cells are sensitized and will be hæmolysed, but at such a slow rate that the infant can excrete the bilirubin so formed at such a rate that severe jaundice does not develop. If the ability to regenerate new red cells is good, anæmia will not appear in such infants. As a rule anæmia develops in the third or fourth week of life, usually of mild degree and requiring no treatment; but occasionally the anæmia may be so severe as to require a blood transfusion. Hæmoglobin values should be determined at weekly intervals in all infants with hæmolytic disease of the new-born who have not been treated with replacement transfusion. One should watch these children carefully in the third week, as the fall in hæmoglobin value may be quite precipitous at this period. If the hæmoglobin value falls below 9 grammes per 100 ml. in the second week, 8 grammes in the third week or 7 grammes in the fourth week, a small transfusion of 100 ml. of whole blood or preferably packed cells should be given. After this age, the infant's bone marrow is functioning well and a rise in hæmoglobin value will occur without recourse to transfusion. Very occasionally, several such small transfusions will be necessary. Iron or other hæmatinics will have no effect and should not be given in these cases.

Summary.

Hæmolytic disease of the new-born has been discussed from the point of view of management. Comments have been made with regard to ante-natal assessment of severity, where the mother should be delivered, whether and when labour should be induced and the indications for replacement transfusion at birth and in the first few days of life. The importance of jaundice in the new-born, the fallibility of capillary hæmoglobin levels in the assessment of severity after birth and the clinical features of kernicterus have been considered. Brief mention is made of hæmolytic disease due to other causes than Rh incompatibility, to the jaundice of prematurity and to the indications for replacement transfusion in these cases. Finally, the anæmia which may occur in the mildly affected infant, who is not severely enough affected to require replacement transfusion, but who may develop anæmia in the third or fourth week, is described, with the treatment necessary.

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HÆMOLYTIC DISEASE OF THE NEW-BORN.[1]

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HÆMOLYTIC DISEASE of the new-born is the generally accepted name for a condition which invariably begins in utero. There are two main types of hæmolytic disease. Hæmolytic disease due to anti-Rh is the one which has received most publicity over recent years in the lay Press. It is the condition which any editor of a women's magazine can always use to fill a few spare pages in an issue, knowing that his or her readers will be mildly terrified. The second form of hæmolytic disease of the new-born, due to anti-A and anti-B, has received little publicity, and consequently does not worry the patient, although it may worry her medical advisers.

The true incidence of the two types of hæmolytic disease of the new-born is difficult to determine from a study of hospital statistics. First, any large obstetric hospital will, and should, have a large number of women who have anti-Rh agglutinins referred for ante-natal care and confinement. This makes the true incidence of the condition amongst pregnant women in general difficult to determine. Secondly, many babies suffer mildly from ABO incompatibility, without the condition being diagnosed. Cases of hæmolytic disease of the new-born due to anti-A or anti-B which are severe enough to require treatment are not common. In a series of 1480 new-born infants, Rosenfield (1955) found three who required simple transfusion, but none who required exchange transfusion. Mollison (1956) states that hæmolytic disease of the new-born due to anti-Rh has a maximum incidence of between one in 150 and one in 200 of all births. Approximately 60% of the infants are sufficiently severely affected to require exchange transfusion. Thus, very approximately, one in 300 of all new-born infants have a sufficiently severe degree of hæmolytic disease due to anti-Rh to require treatment.

Hæmolytic disease of the new-born due to ABO incompatibility has a minimum incidence of one in 150 births; the word "minimum" is used because the estimate is based on the number of infants who develop jaundice. It may be taken as certain that other infants have a mild hæmolytic process due to ABO incompatibility, but never display jaundice. However, only about one in 2000 or less of all new-born infants have a sufficiently severe degree of hæmolytic disease of the new-born due to ABO incompatibility to require treatment.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 29, 1960.

Hæmolytic Disease due to Anti-Rh Agglutinins.

Of the cases of hæmolytic disease due to anti-Rh, almost all are due to the antibody anti-D. Anti-Rh can cross the placenta at a very early stage of pregnancy. Mollison (1956) reports the finding of a direct positive response to the Coombs test in two fœtuses with crown-rump lengths of 30 mm. and 110 mm. respectively, corresponding to approximately 10 and 16 weeks' gestation. This early transfer of antibodies adds to the difficulty in the treatment of this condition.

There have been four major advances in approach to the disease over the past twenty years. The first was the recognition of the Rh factor by Landsteiner and Wiener in 1940. The second was the description by Coombs (1945) of the test, which now bears his name, for the detection of sensitization of human red cells with incomplete Rh antibody. The third was the introduction by Diamond (1947) of exchange transfusion.

The last major advance in the treatment of hæmolytic disease of the new-born is the study of the liquor amnii for detection of the disease and as a guide to the prognosis for the affected infant (Bevis, 1952). Although this investigation is a most valuable adjunct to our treatment, it is not of the same epoch-making importance as the previous three advances.

When we consider the chaotic situation that existed before the discovery of the Rh factor, we realize the progress that has been made in the past twenty years. A great reduction in infant mortality followed the introduction of simple transfusion of Rh-negative blood. However, many babies still died of cardiac failure due to the overloading of the circulation, and many more died of kernicterus on about the third day of life.

The first exchange transfusion was given at the Women's Hospital, Crown Street, Sydney, in 1948. However, it was not until 1950 that the procedure became common enough to warrant inclusion as a separate entity in the hospital's annual medical report.

Bourke (1955) and Stening (1956) have dealt with the treatment of Rh-negative women and their babies at the Women's Hospital, Sydney. In this present paper brief mention only will be made of the methods used, and emphasis will be mainly laid on the results of treatment over the past ten years.

The Mother.

The mother is investigated from the point of view of a history of previous transfusions, the date and place of transfusion, and the previous obstetric history. Also, the mother can give valuable information about the strength of the fœtal movements.

All women at their first ante-natal visit have their blood group determined. Rh-negative women are tested for the presence of anti-Rh agglutinins.

Rh-negative women are tested at the thirty-fourth week of pregnancy for the presence of anti-Rh agglutinins.

In recent years, a spectrophotometric examination is made of a specimen of liquor obtained by abdominal paracentesis at about the thirtieth to thirty-second week of gestation or earlier, depending on the patient's previous history of babies affected by hæmolytic disease. This examination is repeated once, the time interval depending on the original findings.

Premature induction of labour is considered, the decision depending on the patient's previous history of affected infants or stillbirths, and on the concentration of bilirubin and fœtal oxyhæmoglobin in the liquor amnii.

TABLE I.
How Pregnancy was Managed.

Year.	Stillbirths, Hydropic Infants; Mothers Rh-Negative with Agglutinins.	Coombs-Positive Babies; Mothers Rh-Negative with Agglutinins.	Surgical Inductions of Labour.	Medical Inductions of Labour.	Cæsarean Sections.	Neonatal Deaths.
1950–1951	4	21	8	—	—	5
1951–1952	4	34	21	—	—	6
1952–1953	5	38	10	—	—	5
1953–1954	6	33	13	—	—	4
1954–1955	11	40	17	—	—	1
1955–1956	4	50	24	7	2	3
1956–1957	13	46	26	6	2	5
1957–1958	13	51	31	9	4	5
1958–1959	10	54	35	7	2	3
1959–1960	5	67	31	10	11	6
10 Year Period ..	75	434	216 (50%)	For 5 year period, 14·6%	21 (4·8%: 8% in 5 years)	43 (10%)

The Infant.

Immediately after the birth of affected babies, the cord is clamped and the direct Coombs test is applied to the fœtal red cells. A hæmoglobin estimation is performed on peripheral blood or on the cord blood, and a serum bilirubin estimation is made.

In accordance with these results, the treatment of the baby is determined.

In this series of 600 pregnancies, 91 babies (almost one in six) or 15·2% were Coombs-negative, so did not require treatment.

The decision as to whether the baby should be treated by exchange transfusion, simple transfusion or observation depends upon his general condition, the hæmoglobin value and the serum bilirubin level. These have been discussed by Dr. Robertson.

Results of Treatment over a Ten-Year Period.

During the ten-year period from July 1, 1950, until June 30, 1960, 600 Rh-negative women whose serum contained anti-Rh agglutinins have been confined at the Women's Hospital, Sydney. Of these, 75, or 12·5%, were delivered of a stillborn infant. All stillbirths were attributable to the effects of anti-Rh agglutinins; the majority of the hydropic infants were premature. As was mentioned earlier in this paper, 91 or 15·2% of the women gave birth to babies who gave a negative response to the Coombs test, so these were unaffected. The remainder, 434 women, gave birth to living infants who were Coombs-positive, i.e., affected infants. Among these infants, the over-all neonatal death rate was 10% (43 babies) of the babies born alive. This figure includes all the neonatal deaths in the group of 600 mothers, whatever the cause (hyaline membrane disease, cerebral hæmorrhage, etc.). Thus the over-all combined stillbirth and neonatal death rate for the series was 19·7% (118 babies). If Coombs-negative babies are excluded, the mortality rate was 23%.

The Management of the Pregnancy.

Table I shows the management of the pregnancies. Of the 434 patients who were delivered of living infants, 216 (50%) had a surgical induction of labour. No patient with a known intrauterine death had a surgical induction of labour; however, some of these were given medical inductions. Some patients who had surgical inductions

TABLE II
Method of Treatment of Affected Babies.

Year.	Coombs-Positive Babies Born Alive.	Number not Treated.	Number Who had Simple Transfusions.	Number Who had One Exchange Transfusion.	Number Who had Two or More Exchange Transfusions.	Neonatal Deaths.
1950–1951	21	6	4	11	—	5
1951–1952	34	13	7	14	—	6
1952–1953	38	19	6	13	—	5
1953–1954	33	15	5	12	1	4
1954–1955	40	19	1	16	4	1
1955–1956	50	11	5	22	12	3
1956–1957	46	19	0	21	6	5
1957–1958	51	18	4	22	7	5
1958–1959	54	16	7	18	13	3
1959–1960	67	30	6	19	12	6
Total ..	434	166 (38%)	45 (10·3%)	168 (38%)	55 (12·6%)	43 (10%)

before term were also given a supplementary medical induction.

The duration of pregnancy when labour was induced varied with the patient's previous obstetric history and other findings. Some inductions were performed as early as the thirty-fourth week of gestation, others as late as the fortieth week. All patients who had surgical inductions of labour were delivered of a live baby.

Over the past five years, there have been a number of Cæsarean sections performed. In some cases there were other obstetric indications, in others the gravity of the hæmolytic disease was the primary indication for Cæsarean section; again, all these babies were live born.

Some of the babies who were given exchange transfusions were also given simple tranfusions at a later date; these have not been grouped separately, but are included amongst the exchange transfusions in Table II.

Table II shows that there has been some improvement in the survival rate of the affected babies over the ten-year period. Over-all, 50% of the babies born alive required one or more exchange transfusions, and a further 10% required a simple transfusion.

Of the 43 babies that died in the neonatal period, 14 were so severely affected with hæmolytic disease that they died before exchange transfusion could be commenced. Twenty-nine babies died during or after an exchange transfusion. Of these, two babies died during the second exchange transfusion and four died during the first exchange transfusion; in five other cases the exchange transfusion had to be abandoned because of the extremely poor condition of the baby. Two babies died from gangrene of the bowel due to mesenteric embolism following exchange transfusion.

In all, there were 13 deaths which could possibly be attributed to exchange transfusion. However, in 11 of these the babies were very severely affected and would no doubt have died if not given transfusions.

Of the other 16 deaths, two were due to cirrhosis of the liver some weeks after birth. Two babies died of cerebral hæmorrhage due to tentorial tears, and four died from atelectasis. Eight babies at autopsy showed evidence of hæmolytic disease only.

What of the Future?

Over the 1950-1960 decade, 20% of the women who exhibited anti-Rh agglutinins during pregnancy failed in their goal to achieve a surviving infant. The majority of these 118 deaths were directly due to hæmolytic disease; a few were secondary to the treatment given. The obstetrician's main aim is to reduce the high incidence (12·5%) of intrauterine deaths, and to give the pædiatrician a more robust baby.

At present we are using the spectrophotometer, in the hope that we shall be better able to predict in which pregnancies to induce labour and at what stage the pregnancy should be terminated. Unfortunately, the earlier in pregnancy that the baby is affected by the hæmolytic process, the greater are the hazards of prematurity if the pregnancy is terminated.

Although the next decade will see some improvement in the number of babies born alive, until our methods of combating hyaline membrane, atelectasis and other complications of prematurity improve, it will be difficult to produce dramatic improvement in the over-all results. Certainly we shall save some badly affected babies by knowing just when the pregnancy should be terminated, and also other pregnancies will be allowed to go on to term.

In conclusion, it should be emphasized that as far as possible all Rh-negative women who have anti-Rh agglutinins, particularly if a previous baby was affected by hæmolytic disease, should be confined in a large obstetric hospital where there is a special unit for dealing with this condition.

Only by close cooperation between obstetrician, pædiatrician and pathologist will this high figure of 20% fœtal loss be reduced.

Acknowledgements.

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ERYTHROBLASTOSIS FŒTALIS — RANDOM THOUGHTS.[1]

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UNIVERSAL ACCEPTANCE of the necessity for the routine blood-grouping of all pregnant women, coupled with detailed ante-natal serological investigation when indicated, has greatly simplified the problem of anticipation in erythroblastosis fœtalis. The modern programme for management of the affected infant has evolved steadily since Levine introduced exchange transfusion. Technique, mechanics and the effects of apparatus, blood group, donor sex, exchange volume, temperature and anticoagulant types have become known. Speculation upon the place of digitalis, albumin, etc., is occasional still, but basic routines of management, such as that outlined by Dr. Robertson, vary little, and then mostly in detail.

The literature is crowded with an abundance of statistics. Major maternity hospitals today can generally claim excellent over-all figures. There is no doubt that this problem is best handled in such a major unit, where experienced staff can constantly command all the necessary ancillary services. Most of today's preventible tragedies are due to delay, which is synonymous with the lack of these basic facilities, commonly in outlying regions.

For the obstetrician there remains the great riddle of individual prognosis and case management. Herein lies a multitude of intriguing and often unanswerable questions. My remarks are directed towards some of these less frequently discussed facets and are prefaced with an apology for the absence of particular or detailed knowledge of this subject and for the contribution of nothing original, unless it is in the form of dissociated ideas or, rather, disconnected queries.

Though some 98% of erythroblastosis stems from Rh anti-D incompatibility, interest is by no means confined to these cases. As early as 1955 Levine had identified 23 of the 49 then known human blood group factors as causes of erythroblastosis, in addition to the Rh factor.

At the time of conception we know that the group O mother surely has anti-A and anti-B agglutinins, com-

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on September 29, 1960.

monly in high titre; yet only 10% of A B O incompatible matings result in obviously clinically affected offspring. Subclinically, however, some two-thirds of all demonstrable erythroblastotic reactions are stated to be due to A B O incompatibility. Repeated pregnancy fails to produce more than an occasional gravely affected baby, whereas Rh immunization, on the other hand, produces progressively more severe fœtal damage. It would seem interesting, then, to look at some of the differing fundamentals of these two immunization processes.

As the Rh antigen is carried directly on the red blood cells, sensitization to it presupposes exposure of antibody-producing sites to this intracellular agglutinin—again presupposing the necessity not only for entry of the red cells into the maternal circulation, but for their survival there. This happens in every pregnancy, most frequently in the latter weeks, when utero-placental circulatory separation is by the finest of cellular membranes. In the earlier weeks there is a steady red-cell "leak-through", quite apart from the later short, brisk losses into the maternal circulation associated with the trauma of labour, Cæsarean section, etc. When we recall that it is calculated that the renal glomerular membrane itself allows the continual daily loss into the urine of some two million red blood cells, a comparable process is easy to envisage.

We know that A B O incompatibility protects the mother from Rh sensitization by the simple process of the rapid destruction of fœtal cells in a hostile maternal environment before they have the opportunity to sensitize. No one, as yet, has explained the strange paradox that it can be quite impossible, on one hand, to sensitize some 10% of A B O compatible recipients who are Rh-D-negative by repeated transfusions of D-positive cells, whereas on the other hand as little as 0·05 ml. of incompatible blood can, in another individual, produce a high titre of specific antibodies.

What happens in A B O hæmolytic disease of the newborn? With the prevalence of A B O compatible matings the pædiatrician ought, at first sight, to have as many sleepless nights as the obstetrician. The group O mother has antibodies virtually invariably, yet rarely do we see a severely affected baby. The explanation here probably lies in the behaviour of the C antigen and its cross-reacting antibody. Persons of groups A and B share the common antigen C, and it is the behaviour of this antigen and of the anti-C antibody which probably determines the nature of A B O hæmolytic disease. No one of blood group O is born with anti-A or anti-B agglutinins; yet all, except those with agammaglobulinæmia, rapidly develop them. Anti-A and anti-B agglutinins, referred to as "naturally occurring", are in reality immune antibodies. They develop in response to sensitization by A and B antigens present in plants, bacteria, foods, protozoa, etc., with which we are in constant contact — hence they are "heteroimmune" antibodies. What probably happens when an incompatible A B O mating causes trouble is that the titre of anti-C in the mother rises in response to isoimmunization. It is anti-C antibody, produced thus, in univalent form, which readily crosses the placental membrane to affect the baby's cells.

This brings us to an interesting point of behaviour difference between A B O and Rh sensitization. The Rh antibody we know has no direct effect on any of the fœtal tissues or organs — it attacks only the red cells. In the Rh-affected fœtus there is, in utero, a progressive and profound anæmia, which commences, strangely, not until after the eighteenth week or so (though Rh-affected cells themselves have been demonstrated in the blood of an embryo as early as the twelfth week), and which can result in cardiac failure, hydrops and stillbirth. On the other hand, an A B O affected infant very rarely shows such anæmia, though after birth it is capable of the same rapid extreme hæmolysis, with the same possible neurological sequelæ as its Rh-affected counterpart.

In the test tube the cells are both found similarly coated with an antibody; however, nature detects a difference. Again, the addition of anti-Rh antibody to incompatible cells *in vitro* normally causes agglutination. However, fœtal cells so coated with anti-Rh antibody that they may in fact produce a false Rh-negative reaction are not, *in vivo*, agglutinated. Nor are they hæmolysed; nor is there any increase in fragility. The spleen, nevertheless, recognizes their abnormality and removes them.

How is it that hæmolytic disease can affect the first baby in an A B O incompatible mating? First, let us remember that 80% of group A and group B persons are secretors and have the anti-A or anti-B with concurrent anti-C antigen in their saliva, sweat, urine and, perhaps, most body fluids. Unlike the Rh antigen, confined to the red cells, the ubiquitous C, along with its A or B, diffuses readily and constantly from the fœtus, and its by-products, to sensitize the group O mother from the earliest months of the first incompatible pregnancy.

Strange, then, that A B O hæmolytic disease in severe form is not more common — is not almost the rule in A B O incompatible matings. Perhaps the fact that there are various types of anti-C antibody, differing in affinity for the antigen, contributes. Again, it is suggested that a degree of heterospecificity can dilute the antibody-antigen reaction.

We ought always to remember the potential sensitizing ability of pooled plasma, convalescent measles serum, hormones from human urine, etc. Isoimmune reactions following their use may perhaps raise specifically that univalent anti-C fraction which is potentially troublesome.

Of interest in the field of infertility is the recent work of Behrman *et alii* on the significance of the presence of antigens in spermatozoa, and the effect on these of antibodies present in the wife's cervical mucus in A B O incompatible sterile matings.

In utero, the fœtal danger is progressive anæmia. Once the baby is born, the problem is the disposal of bilirubin. Bilirubin disposal in utero apparently causes little difficulty. Presumably the mother excretes it; strange how the albumin-bound molecule, which cannot traverse the renal or hepatic barrier, has no difficulty with the placental barrier. Is it because there is an efficient glycuronyl acid transferase system in the placenta, which conjugates the bilirubin, making it readily diffusible? (How interesting it would be to have the time and facilities to investigate the maternal output of, say, fœtal and urinary bile pigments in a mother, heavily sensitized with an incompatible pregnancy.)

Excretion may even bear some direct linear correlation to the degree and rapidity of fœtal hæmoglobin destruction. To make these estimations, if the correlation was so, would be even simpler and more comfortable for the patient than amniotic tapping.

No baby, no matter how severely affected, is born alive and jaundiced. Many babies, however, have bilirubin levels which would cause extreme jaundice in adults. Presumably bilirubin in blood and tissues is transferred to stain the skin in response to some photosensitive mechanism; it is noticeably slower in skin creases, under strapping etc.

The neonate's difficulties in bilirubin handling are twofold. There is, firstly, a rapid increase in the rate of bilirubin production, and, secondly, at least for some days, there is inadequate hepatic glycuronyl acid transferase activity to cope with its conjugation—a problem, of course, much worse in the premature infant. It is well to remember that the glycuronyl acid transferase system participates also in the metabolism of hormones, steroids and drugs—for example, morphine, chloramphenicol and sulphonamides.

Hence we ought to think about medicaments and antibacterials for mother and baby when hæmolytic disease is involved. We know the "Gantrisin" effect in increasing neurological sensitivity to bilirubin, and one cannot help but wonder about the possible importance of extrahepatic glycuronyl acid transferase activity, the significance of normal gastro-intestinal flora, etc.

The obstetrician's basic problem with hæmolytic disease in the new-born consists of the management of the known

sensitized pregnant mother—a problem which resolves itself into two simple questions: (i) Can anything be done to moderate the severity of the disease process or to protect the fœtus from hazard till it is mature enough for safe delivery? (ii) In the absence of the ability to limit or negate the sensitization process or to protect the fœtus itself, what can we do for those unfortunate women who belong to the 30% who have a bad prognosis—who have had a severely affected infant, a hydropic infant or stillbirth?

An affirmative answer to the first question would demand the isolation of the Rh hapten. As early as 1947 and as late as 1956, Bettina Carter believed this had been done. Unfortunately her presumption was incorrect. When considering the possibility of inactivating antibody by Rh hapten (or any other substance), it is well to remember the magnitude of the project. Since the demonstration of the half-life of the Rh antibody and the observation that even extreme titres of maternal antibody are commonly preserved, unreduced, without further antigenic stimulus, for as long as three years, one can well imagine the enormous potential antibody-productive capacity of the sensitized woman.

Competition of antigens with pertussis vaccine and the exhibition of cortisone have both failed to prevent hydrops and stillbirth. Prophylactic use of vitamin C, riboflavine and methionine was, from the beginning, doomed to failure by virtue of false premises. Attempts at protecting the fœtus from anæmia with vitamin B_{12}, liver, folic acid and vitamins have been, naturally enough, unsuccessful.

To the second half of our question there is only one answer. We can, and sometimes must, remove the fœtus from its unsatisfactory environment. This poses a still more difficult dual question: How are we to determine which fœtus is in imminent danger? And, again, when is the optimum time for its removal from its hazardous environment? Several factors are worthy of consideration in attempting to find the answer.

By serological investigation and the predication table, we may show that the hazard is reduced by 50% if the husband is demonstrated to be heterozygous—a genetic state absolutely confirmed if one of his offspring is found to be Rh-negative.

Statistics have some general uses, and we know the probabilities. In Rh-incompatible pregnancies, which follow the birth of one affected baby, 50% of children will survive; after a live-born affected baby, which subsequently dies, 20% survival can be expected—a figure which drops to 10% after a stillbirth or previous hydrops.

Serum titres constitute a somewhat vexed subject, which is not quite so closed as some may presume. I hesitate to believe that we ought completely to disregard antibody titres. We know the variables and the fallacies—temperature, incubation time, freshness of cells, mode of end point titration, etc. These are controllable variables. Parallel titration of frozen serum specimens collected serially and examined collectively may well be of more definite significance. It would be difficult in a case such as ours to disregard entirely major titre increases in the latter weeks of an incompatible pregnancy.

At least we know that high titres are usually associated with severe disease, and vice versa. Diamond himself draws direct conclusions from 350 odd cases, and notes a fourfold increase in the ultimate stillbirth rate amongst babies alive at 37 weeks, when the titres were high and low respectively. With a history of a previous stillbirth or hydrops, corresponding survival rates with high and low titres were 35% and 20%.

We are in a state of hopeful enthusiasm about amniotic taps. This subject is by no means a new one, and was being hotly debated some ten years ago. As early as 1952 (and more recently in 1956), Bevis published observations on the composition of the liquor amnii in Rh-affected women and attempted to correlate certain characteristics with fœtal prognosis. Others have subsequently contributed in this field (Walker, Wild, Abbis, Terry, Barnes), and recently some work has been done here in Australia.

The facts can be summarized as follows:

1. If amniotomy is performed at the thirty-second week, and of necessity before the thirty-fifth week, a prognosis as to whether or not the baby is Rh-affected can be made accurately in 90% of cases. After the thirty-fifth week, opalescence and turbidity in the fluid so interfere with the interpretation of the tests that accuracy is reduced to below 50%.

2. There is evidence that the spectral absorption curve may offer a reliable guide to the subsequent development of kernicterus.

3. It is suggested that an even better idea is obtained by considering the amniotic concentration of the pigments—unconjugated bilirubin and fœtal oxyhæmoglobin. It will be recalled there is some evidence to suggest that fœtal oxyhæmoglobin may play a part in neurological damage. High levels of bilirubin and oxyhæmoglobin suggest the likelihood of kernicterus, whilst a high bilirubin level and normal oxyhæmoglobin level suggest erythroblastosis. It is probable also that early amniotic appearance of evidence of severe hæmolysis presages intrauterine death.

4. Amniotic proteins are believed to have prognostic significance. For some years it has been well known that the protein content of liquor amnii rises with the presence of fœtal hydrops. A great deal of work has been done, but little agreement reached. Four proteins are universally demonstrable. Wild holds that, at 32 weeks, alpha-2 globulin is invariably absent except in established hydrops. Grossly different levels of amniotic fluid protein are obtained when paper and free electrophoresis are the analytical methods used. Total protein levels of 300 mg. and even 1000 mg. per 100 ml. have been reported with hydrops. Barnes, who reported this latter level, found with another affected baby a rise in protein content from 225 mg. per 100 ml. at 32 weeks to 630 at 36 weeks.

5. Antibodies are demonstrable in the liquor. Though anti-D has been found in the liquor, and is, in fact, usually demonstrable with maternal titres above 128, it is sometimes undetected. The high liquor concentration of 128 has been recorded, again in association with hydrops.

This, then, is our armamentarium. With these crude and incomplete prognostic methods we must attempt to determine the probable fate of the baby in utero. We decide that the fœtus is affected, that the pregnancy ought to be terminated and that the optimum moment for termination has come. Having weighed the risks and decided that a particular fœtus must be removed from its environment, let us proceed towards this end with determination: induction of labour first by all means, but planned, purposeful, determined induction rather than historical gesturing.

The pædiatrician can save for us up to 95% of babies delivered alive in reasonable condition. The management of hæmolytic disease in the living infant is established now on a sound footing. Spurious arguments about treatment and the prevention of kernicterus have been settled. The problem of the management of prematurity is surely within the scope of the pædiatrician. Let us attempt, therefore, to deliver to him babies at least alive, even though premature, rather than macerated stillborn infants and hydropic buddhas.

FIVE YEARS' CONSERVATIVE OBSTETRICS.

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THE British and Australian medical journals have, during recent years, published various analyses of obstetric results in isolated communities and districts. I believe the results here are also interesting enough to submit for publication, for the following reasons: (1)

We are in the unique position of being the only hospital serving a district in which no private obstetric practice is carried out. We were the only hospital south of Rehovot, a distance of about 300 kilometres. Eilat during these years had no hospital. Rehovot accepted patients to about as far south as Pleugot until we were forced by lack of bed space to restrict our district. (ii) Our patients come from at least 38 different countries, as follows: North and South America, Afghanistan, South Africa, Algeria, Australia, Bedouin (Israelis), Belgium, Bulgaria, Cochin India, Czechoslovakia, Egypt, England, France, Germany, Greece, Holland, Hungary, India, Iraq, Ireland, Israel, Italy, Jordan, Lebanon, Morocco, Persia, Poland, Roumania, Russia, Spain, Sudan, Switzerland, Tripoli, Tunisia, Yemen, Yugoslavia. (iii) One person was in charge of all the confinements during the time under review, with the exception of those occurring during periods of absence of two weeks, three weeks, four weeks and three months during these years.

The population expanded rapidly, from 14,500 in the town and 25,987 in the surrounding district at the end of 1952, to 24,244 and 44,232 in town and district respectively at the end of 1956. The population at the end of June, 1958, had reached 40,000 in the town and 80,000 in the district, and our births average over 200 per month; but I am not submitting figures after January, 1957, when I ceased to work alone.

It seems relevant to consider something of the background of the work. The obstetric department of the hospital was housed in a separate small building, which had served as the local Health Department in the days of the British Mandate. There were officially 26 beds, which were adequate for the first year; but with the rapid growth in the population and no corresponding increase in accommodation, the department soon became grossly overcrowded. At one stage, when we had over 60 patients, as there was no more floor space on which to place stretchers, an emergency tent was erected to take the overflow.

Patients went home normally on the fourth day after delivery, the day of delivery not being counted. No patient was discharged from hospital if she had any rise in temperature or if her baby was not gaining weight, and no baby was discharged until he weighed 2·5 kg. During times of great pressure on the beds (and this occurred frequently in 1956), patients were discharged on the third day after delivery if the above-mentioned two factors held good.

When I first commenced to work here, no gowns were worn by the midwives and no sterile drapings were used on the patients. Antibiotics were used very freely. A pack was immediately introduced, consisting of an autoclaved bundle containing a gown for the midwife, and for the patient leggings, undersheet and the usual towels and dressings associated with modern obstetrics.

During the period under review — January, 1952, to January, 1957, inclusive — there was a total of 7369 deliveries with four maternal deaths. Of these patients, 1986 were primiparæ and 5383 multiparæ. In the tables, "primipara" refers to the first birth, not necessarily to the first pregnancy. The results of these confinements are summarized in Table I and then discussed briefly.

Twin Births.

The usual figure for the incidence of twin births quoted in textbooks is about one in 80. On this allowance we had somewhat above the usual average (about one in 70), but it is generally considered that primitive communities and grand multiparæ produce more twin births, and that is in keeping with much of our material. We had one case of triplets.

Episiotomies and Perineal Tears.

According to the tradition at this hospital, episiotomies were performed by the midwives in most cases. I am aware that in many hospitals routine episiotomies are carried out for primiparous deliveries, but I thoroughly disapprove of any routine interference, and the small number of primiparæ requiring suture of the perineum when episiotomy was not carried out seems to confirm the opinion that this small operation is by no means always required, and I believe it was performed more often than was necessary here. I realize that some authorities consider that an episiotomy tends to minimize the incidence of prolapse in later life, but this is not proven.

Of the primiparæ reviewed here, 24·3% underwent episiotomies and 15·6% had perineal sutures. This figure includes all cases of suture, even if only one stitch was required, but those in which the midwife inserted a Michel clip or two for a superficial skin laceration have not been included.

TABLE I.

Summary of Results, January, 1952, to January, 1957.

Table IA.
Details of Confinements.

Abnormalities in Confinements.	Number of Cases; Percentage of Total.		Incidence in Primiparæ; Percentage of Primiparæ.		Incidence in Multiparæ; Percentage o Multiparæ.	
Twin births	104	(1·41)	19	(0·96)	85	(1·58)
Episiotomies	586	(7·95)	483	(24·32)	103	(1·91)
Sutures	468	(6·35)	310	(15·61)	158	(2·93)
Cervical tears	34	(0·46)	13	(0·65)	21	(0·39)
Forceps deliveries	293	(3·98)	222	(11·28)	71	(1·32)
Breech deliveries	184	(2·49)	59	(2·97)	125	(2·32)
Toxæmia	67	(0·91)	28	(1·41)	39	(0·72)
Pre-eclampsia	7	(0·10)	5	(0·25)	2	(0·04)
Eclampsia	8	(0·11)	7	(0·35)	1	(0·02)
Manual removal of placenta	89	(1·21)	29	(1·46)	60	(1·11)
Placenta prævia	32	(0·43)	5	(0·25)	27	(0·50)
Rh-negative blood	361	(4·90)	84	(4·23)	277	(5·15)
Positive Wassermann reaction	12	(0·16)	2	(0·10)	10	(0·19)
Cæsarean sections	47	(0·64)	18	(0·90)	29	(0·54)
Prolapse of umbilical cord	18	(0·24)	4	(0·20)	14	(0·26)
Blood transfusions	124	(1·68)	28	(1·41)	96	(1·78)
Normal confinements	4935	(66·82)	670	(33·73)	4265	(79·23)
Total confinements	7369	(100)	1986	(100)	5383	(100)

Sutures were all of catgut, usually No. 0, and were inserted under local anæsthesia obtained with a 2% solution of "Ethocaine".

Of the multiparæ, 1·9% were subjected to episiotomy, and 2·9% suffered perineal lacerations — a very marked contrast to the primiparæ.

Over the years we had only two cases of third-degree tears.

Laceration of Cervix.

Until I worked in this country I had not seen a spontaneous laceration of the cervix during labour. If there were any, they were not revealed by post-partum hæmorrhage, I have never carried out routine post-delivery examinations in the labour ward, but in the 34 cases recorded here the patients had severe post-partum hæmorrhages that necessitated examination. By experience one learnt that post-partum hæmorrhage associated with a well-contracted uterus is an almost certain diagnosis of a torn cervix.

This figure of 34 cases, although it is only 0·46% of our total deliveries, seems to me a high number. Thirteen of them occurred in primiparæ and 21 in multiparæ. Of the cases in primiparæ, seven were associated with forceps delivery and one with manual removal of an adherent placenta — that is, more than half the cases were associated with interference, which is in conformity with textbook statements. But what of the five which were associated with spontaneous delivery? Amongst the multiparæ, one tear was associated with an occipito-posterior spontaneous delivery, one with internal version from the transverse position, two with breech presentation, one with forceps delivery

and one with manual removal of the placenta, leaving 15 which were associated with spontaneous delivery. Fifteen multiparæ, together with five primiparæ, make 20 cases of ruptured cervix with no interference whatever. Amongst the cases that were associated with forceps delivery I am not convinced that the rupture was necessarily due to the mode of delivery, as in several cases there was a sudden spontaneous flow of bright blood late in labour, before forceps had been applied, or indeed any vaginal examination had been performed. Looking back on these cases after the rupture was detected, I concluded that the cervix had torn at this time. I cannot prove this conclusion, but as I have never applied forceps unless the cervix was fully dilated, it seems to me a reasonable supposition. The only common factor observed in most of these

Table Ib.
Outcome of Confinements.

Outcome.	Number of Cases. (Total 7475.)[1]	Primiparæ. (2005)	Multiparæ. (5470)
Live births	7354	1969	5385
Premature births	555 (7·55%)[2]	212 (10·77%)[2]	343 (6·37%)[2]
Stillbirths	121 (1·62%)[2]	36 (1·80%)[2]	85 (1·56%)[2]
Neonatal deaths (defined as one week)	113 (1·54%)[2]	30 (1·52%)[2]	83 (1·54%)[2]
Neonatal deaths (defined as one month)	147 (1·99%)	46 (2·34%)	101 (1·88%)
Maternal deaths	4	1	3

[1] Total births including triplets.
[2] Expressed as percentage of live births.
[3] Expressed as percentage of total births.

deliveries was an abnormally quick labour, and subsequently an attempt was made to avoid a torn cervix by giving extra sedatives in such cases.

Simple suture, the needle being inserted about 0·75 cm. from the torn edge, with an occasional mattress suture if the bleeding was troublesome, or if the torn edges were too friable, proved a very satisfactory means of repair. Number 1 plain catgut was generally used, and in no case did the wound fail to heal by first intention. After six weeks it was frequently difficult to believe that any tear had been present, the cervix presenting as a perfectly smooth, normal cone. One such patient, whose cervix was so perfectly healed that I checked my notes against her name to make sure that there had been no error, had a second rupture again in her next labour. To my knowledge this was the only case of recurrence we had, although women with previous cervical tears were delivered again.

Forceps Deliveries.

We had a total of 293 women delivered by obstetric forceps, an over-all average of 3·98%. This represented 11·28% of primiparæ and 1·32% of multiparæ. There were undoubtedly cases of forceps deliveries here that would have been considered suitable for Cæsarean section at other hospitals (see later).

Prolapsed hand, prolapsed cord and face presentation were among the rarer indications, accounting for three primiparæ and seven multiparæ. Maternal factors such as mitral heart disease, asthma, eclampsia, preeclampsia and toxæmia accounted for a further nine primiparæ and one multipara. The remaining forceps extractions were performed for the following reasons. For fœtal distress 108 primiparæ and 37 multiparæ were delivered by forceps — this was the biggest single cause. The next cause numerically was slow progress of labour, accounting for 79 primiparæ and 23 multiparæ. For uterine inertia seven forceps extractions were performed in primiparæ, and for maternal distress seven also in primiparæ. In 12 cases the reason was not recorded, nine of these being in primiparæ and the remaining three in multiparæ. In all 222 forceps extractions were performed in primiparæ and 71 in multiparæ.

Fœtal Distress.

In the list of reasons for forceps delivery, if fœtal distress and slow progress together were the indications for termination of labour by forceps, fœtal distress only has been tabulated, as, in any event, this would have been enough grounds for terminating the labour as speedily as possible. When conditions were favourable, it was the policy to deliver the baby with forceps at the first signs of fœtal distress rather than to wait until the child was *in extremis*.

Slow Progress.

If the head of the child was visible and the labour did not progress, it was the practice not to wait until fœtal distress or maternal fatigue resulted, but to deliver the patient with outlet forceps. This spared both mother and child unnecessary stress. With few exceptions, only "low forceps" deliveries were carried out. A few "mid-forceps" applications were performed, but no "high forceps". Some of the multiparæ listed as having slow progress were delivered by forceps for teaching purposes.

Breech Deliveries.

In this country, breech delivery is known as pelvic delivery. There were 184 cases of pelvic delivery in all, a percentage of 2·5. In the ante-natal clinic I perform version in all "easy" breech presentations, but as the custom is frowned on in this country, I no longer do this in "difficult" breech presentations. Also, with increasing experience one does bceome less worried about a breech delivery. However, I still consider external version during pregnancy completely justified.

Version to Breech.

Amongst the breech deliveries are included 16 cases of internal or combined internal and external version, 10 of these versions being performed for a prolapsed arm, with or without prolapsed umbilical cord. I am aware that it is generally taught that version is not the ideal treatment for a prolapsed hand or arm, and it is said that it is easy to replace the arm and push down the head. I have rarely succeeded in doing this, and when the cord as well is prolapsed there seems no justification for making the attempt. Also most teaching is against extraction after version; but as this was always done for the sake of the baby, it seemed desirable to complete the delivery as soon as possible in each case, and I had no reason to regret doing so. There was a total of four fœtal deaths in these 16 cases, one of which was of a macerated fœtus weighing 800 grammes. The other three cases of stillbirth occurred in multiparæ, one after version from the transverse position (the baby weighed 2500 grammes), one in a case of hydramnios with prolapsed hand and cord of a full-term infant (unweighed) of a tuberculous mother, and the third after version for prolapsed cord of a child weighing 3500 grammes.

The only two versions done in primiparæ resulted in living babies weighing 3650 grammes and 3850 grammes respectively, so although it it an undesirable manœuvre, version is well justified in certain circumstances. These two versions were performed for prolapsed arm in the first case and for transverse lie in the second case.

Toxæmia, Preeclampsia and Eclampsia.

By no means all the patients attended ante-natal clinics. In the early days I carried out all the ante-natal work myself, but the whole concept of ante-natal supervision was foreign to a large number of the patients, and much propaganda was needed to induce them to attend the clinics. In later years the Health Department opened clinics in numerous villages with visiting doctors. As the years went by, the general practitioners became more aware of the danger, symptoms and signs of

toxæmia and sent an increasing number of patients to my clinic for consultation and/or admission to hospital.

The number of cases of toxæmia assessed according to a rigid standard of blood pressure of over 120/90 mm. of mercury would have been in excess of what is recorded here. No routine standard was adopted, each patient being assessed individually, and many patients who were undoubtedly toxæmic received treatment in the ante-natal clinic and came to delivery without being labelled toxæmic. Obviously such a method can be practised safely only by someone with experience in dealing with such cases. It was feasible here, as I was also responsible for the same patients in the labour ward. Also the bed situation in the hospital and the women's reluctance to leave their families for more than the minimum time made ambulatory treatment necessary whenever this was reasonably safe for the patient. In short, these figures do not give a true picture of the incidence of toxæmia in the pregnant population of this district. The patients with preeclampsia had blood pressures of over 180/120 mm. of mercury with albuminuria, and were detected in the ante-natal clinic and admitted to hospital. All were treated conservatively and were delivered of live babies.

There were no maternal deaths in the eight cases of eclampsia, and we were lucky in that all the infants were born alive with the exception of one macerated seven-months fœtus. A set of premature twins weighing 1750 grammes and 2150 grammes died at nine and 13 days of age respectively. The other babies were discharged alive and well.

It is worthwhile to glance at the yearly incidence of eclampsia. The numbers are very small, but the trend in the table emphasizes the modern concept that it is largely a preventable disease. A greater number of toxæmic patients have been referred to hospital for admission, and in this way their progress to eclampsia has undoubtedly been controlled.

The yearly incidence was as follows: in 1952 there were three cases in approximately 1136 confinements; in 1953, four cases in approximately 1077 confinements; in 1954, no cases in approximately 1272 confinements; in 1955, one case in approximately 1661 confinements and in 1956, again no cases in approximately 2043 confinements.

The case in 1955 was that of a girl, aged 17 years, with a small pelvis, who had two fits during labour and was delivered by Cæsarean section of a living child weighing 3690 grammes. She had attended the ante-natal clinic only once at six months' gestation.

The ages of these mothers ranged from 17 to 30 years, and the weights of the babies from 1750 grammes (one of the twins), to the infant weighing 3690 grammes, who is mentioned above. With the exception of one in 1953 who had a post-partum fit, all the eclamptics were primiparæ.

Manual Removal of Placenta.

This was carried out on three or four occasions as a routine after forceps delivery, if one anticipated any complication, or if one wanted to complete the delivery whilst the patient was under the anæsthetic, as in the case of one of the eclamptics.

Most of the other manual removals were performed for excess bleeding in the absence of signs of placental separation, and on a few patients who were admitted to hospital after delivery at home and who came with the placenta still *in situ*. However, the majority of the latter responded to catheterization and intravenous injection of "Pitocin" followed by the application of a little fundal pressure.

Placenta Prævia.

Of the five cases of placenta prævia occurring in primiparæ, one was a central placenta prævia, two were marginal and the sites of the other two were not specified. Three of these women were delivered by Cæsarean section with two resultant fœtal deaths.

Of the multiparæ, 14 were delivered by Cæsarean section, and there were two resultant fœtal deaths, one baby dying before and one during the operation. Amongst the multiparæ there were five cases of central placenta prævia, 10 cases of marginal placenta prævia, and three cases of lateral placenta prævia, while the sites of the remaining nine cases were not specified. As far as possible, after the initial bleeding, conservative measures were adopted until the child was viable, but out of the 32 cases there were eight fœtal deaths as a result of this major complication of pregnancy, only one of which was that of a full-term infant.

The weights of the others were between 2450 and 900 grammes. Apart from the degree of prematurity, the babies delivered from mothers who had suffered from placenta prævia seemed unduly fragile.

Rh-Negative Blood.

Of the patients whose blood we examined, 4·9% had Rh-negative blood, but this does not indicate the percentage of such women delivered, as in many cases blood typing had not been carried out before the patients' admission to hospital and was not done there. In later years a Coombs test was performed on the cord blood of all babies born to mothers whose blood group we did not know; and naturally it was performed in all cases in which the mother's blood was known to be Rh-negative.

We had 10 cases of erythroblastosis. Two of these babies were born to primiparæ, one was affected by hydrops fœtalis, and the other, born alive, was sent elsewhere for exchange transfusion, and I am unaware of the outcome. Nor do I know the past history of these two primiparæ. The remaining eight babies were born to multiparæ and all received exchange transfusions. Two of these babies were premature and died during the transfusion.

No inductions of labour were carried out in cases of sensitized women with Rh-negative blood, as I had followed the literature of the British school which tended against inductions, considering that a premature baby sensitized to the Rh factor was more difficult to handle than a full-time affected infant. Our two deaths of premature infants tended to confirm this, but our numbers are too small to give any true picture.

Positive Wassermann Reaction.

There were remarkably few cases of positive Wassermann reactions—actually only two in primiparæ and 10 in multiparæ. This probably does not represent the complete total, as Wassermann and Kahn tests were performed routinely only on the patients who attended the ante-natal clinics although they were also done if there was any indication for them after delivery. However, the incidence of infection amongst pregnant women here is obviously very low, and we had no case of congenital syphilis.

Cæsarean Sections.

Through reasons unfortunately beyond my control the number of Cæsarean sections performed during this period was the irreducible minimum, being 0·64% of the total confinements.

The indications for which the operation was performed are as follow: for placenta prævia, 17 sections were performed; for obstructed labour or cephalo-pelvic disproportion, 11; for sterility plus primary uterine inertia, 6; for sterility plus age, 1; for deformed pelvis, 3; for accidental hæmorrhage, 2; for eclampsia plus small pelvis, 1; and for fœtal distress plus social reasons, 2. There were also four elective repeat sections. In all, this represents a total of 47 Cæsarean sections.

Only two repeat sections were done because the first delivery was by Cæsarean section. In both cases the

original operation was performed elsewhere and the patients demanded it the second time. In two other cases second elective sections were performed, as it was known that the patients could not be delivered *per vias naturales*. In no other case was a Cæsarean section carried out simply because the previous delivery was by section.

This necessitated more than normal supervision of the labour, but in no case was there cause to regret the decision to treat the patient conservatively.

One other patient was subjected to Cæsarean section for a deformed pelvis. As she was transferred from here to Hadassah Hospital, Jerusalem, I have not included her in the foregoing numbers.

Prolapse of the Umbilical Cord.

There were 18 cases in all of prolapsed umbilical cord, four occurring in primiparous births with one baby still-born after forceps delivery, and 14 occurring in multiparous births. The fœtal wastage was high in this serious calamity, only 10 babies being delivered alive, the remaining eight being still-born. Of the 10 live babies four were delivered by forceps, one was delivered after version and spontaneous vertex delivery followed reposition of the cord in the remaining five.

Of the eight still-born babies, one was dead before labour commenced and one was presenting by the pelvis; two were delivered after version and two after the application of forceps; and two were born spontaneously after reposition of the cord.

Hæmorrhages and Blood Transfusions.

The number of cases of post-partum hæmorrhage has not been recorded here, as excess blood loss was not always reported at once, and no measurements of the quantity were made, therefore no useful figures are available. Transfusions were given for various reasons, as follows: for hæmorrhage, 18 primiparæ and 44 multiparæ received transfusions; for marked anæmia, 6 primiparæ and 26 multiparæ; and for reasons not stated, 4 primiparæ and 26 multiparæ; this makes a total of 28 primiparæ and 96 multiparæ who were transfused in the period under review.

Amongst unusual causes of hæmorrhage in labour was one case of severe epistaxis and one of ruptured vaginal varicosities. One severe hæmorrhage occurred in the case of a woman with a retained placenta, who was prevented by her neighbours from travelling to hospital on a holy day. The other causes of hæmorrhage were uterine atony, ruptured cervix and placenta prævia. Patients who underwent Cæsarean section and received blood transfusions during operation have not been included. Many of our patients, especially the grand multiparæ, suffered from anæmia, but usually only those with the more severe grades received transfusions, as their husbands and relatives refused to give blood donations. For emergencies, blood was always made available from our small blood bank.

Medical Induction of Labour.

Only on one occasion during these five years was a surgical induction of labour performed, and that was for a placenta prævia in a multipara at about eight months' gestation. This resulted in a baby weighing 1840 grammes which lived.

On only 10 occasions during this period was a medical induction instituted, and in most cases this was for premature rupture of the membranes with primary uterine inertia in full-term pregnancies, with the exception of one case of twin pregnancy in which there was an interval of four days between the delivery of the first and second twins. This case will be reported in another paper.

Only a very small proportion of our non-European patients could tell us when their last menstrual period occurred; therefore, although much has been written about induction of labour for post-maturity, it is clear that we could not follow such teachings, and there were very few cases indeed in which it appeared that we lost a baby that might have been saved by induction of labour a week or two earlier.

"Pitocin" Drip Therapy.

Apart from the above, there were 23 patients who received intravenous injections of "Pitocin" by the drip method, 12 being primiparæ and 11 multiparæ. The indications were as follows: for premature rupture of membranes with uterine inertia, three primiparæ and five multiparæ received infusions; for uterine inertia, nine primiparæ and four multiparæ; for premature separation of the placenta, one multipara; and for the second of twins, one multipara.

It has been suggested that there were unusually few cases of primary uterine inertia amongst the patients here, as manifested by the very moderate use of medical inductions of labour and of "Pitocin" drip infusions. It is well known that the majority of cases of primary uterine inertia are due to fear and anxiety on the part of the mother. It may almost be termed a psychosomatic manifestation. It was the policy here to avoid, as far as possible, admitting primiparæ too early in labour. Whenever possible they were sent home with the advice: "Finish the laundry work and make a cake for your husband before you come back to hospital." In the many cases in which the patients had come from a distance, they were told to do some shopping, walk around the town or visit some friends. When, after admission, labour was slow in starting, the women were put in the general ward instead of in the labour ward, and were not encouraged to think that their labour had commenced. In my opinion many obstetric abnormalities are caused by unnecessary and untimely interference with what is usually a normal process. This does not mean that laziness and stupidity can be used as substitutes for patience, but intelligent waiting solves most obstetric delays.

Premature Births.

There was a total of 555 premature births, which means that 7·42% of the total births were premature. A weight of 2500 grammes was taken as the border-line between prematurity and full term, irrespective of the period of gestation, which, as I mentioned above, was often unable to be ascertained.

There is such a great variation in the incidence of prematurity quoted in different articles and in different countries, and prematurity depends on so many unknown and unproved factors, that no attempt has been made to compare our numbers with any other figures available to me, but it is interesting to note that here more primiparæ gave birth to premature babies than did multiparæ, which is in conformity with findings elsewhere.

Fœtal Mortality.

The distribution of fœtal wastage is shown in Table II.

Further details of the distribution of fœtal wastage are shown in Table III.

Of the total premature births, 106 were among twins; in 36 cases both twins were premature and in the remainder one partner weighed over 2500 grammes. Amongst the premature babies that were born alive and died there were 10 cases of major congenital abnormality incompatible with life, such as anencephalus, diaphragmatic hernia and œsophageal stricture, and many babies weighing under 1500 grammes.

Amongst the full-term babies that were born alive and died, 19 had similar major congenital abnormalities that precluded them from living, including severe spina bifida, anencephaly and cardiac, renal and bowel abnormalities of major degree.

Amongst the still-born babies of both groups (premature and full-term), there were 12 fœtuses with

gross obvious abnormalities, and many were macerated. Fourteen were born outside hospital and brought in dead.

As is usually the case, prematurity was the greatest cause of mortality amongst our babies.

The incidence of major malformations here is rather high (15·3% of the total fœtal deaths), especially as it refers to obvious malformations. We rarely performed autopsies here, owing to lack of personnel; therefore it is not known what proportion of the apparently normal infants who failed to survive had covert abnormalities incompatible with life. This applies particularly to the deaths amongst the premature infants, in whom it is very possible that the concealed abnormalities were more numerous than the manifest ones. It is generally considered that the over-all incidence of congenital malformations amongst babies stillborn and dying in the neonatal period is something over 14%, and this refers to autopsy examinations.

TABLE II.
Total Fœtal Wastage.

Outcome.	Number of Cases.	Rate per 1000 Births.
Live births	7354	—
Stillbirths	121	16·2 (total births)
Neonatal deaths (defined as one month)	147	19·9 (live births)
Total loss	268	36·4 (live births) 35·9 (total births)

TABLE III.
Fœtal Wastage in Full-term and Premature Births.

Fœtal Loss.	Full-term Births.			Premature Births.		
	Total.	Primiparæ.	Multiparæ.	Total.	Primiparæ.	Multiparæ.
Stillbirths	84	21	63	37	15	22
Neonatal deaths (defined as one week)	43	9	34	70	21	49
Neonatal deaths (defined as one month)	53	14	39	94	32	62

It is interesting to note that the number of major congenital abnormalities is higher in the multiparæ (0·6%) than in the primiparæ (0·4%). The same applies to macerated fœtuses. This is in contrast to premature births, whose incidence was greater amongst primiparæ.

Hydrops fœtalis has not been included amongst the congenital abnormalities.

If we exclude from the neonatal deaths the 29 cases of major congenital abnormality, we are left with a total of 118 deaths, or a corrected neonatal mortality rate of 1·6%, which includes all the premature babies.

Of the full-term, normal babies born alive, only 37 failed to survive the neonatal period from the obstetric point of view. I have no record of babies who may have been admitted to the pædiatric department days or weeks after their discharge from the obstetric department.

It is noteworthy that we had no separate premature nursery, no air-conditioning or cooling apparatus and no means of isolation except the placing of a card on the infant's cot labelling it infectious.

Maternal Mortality.

During the whole period under review we had four maternal deaths. The clinical records of these patients are summarized as follows:

A. A multiparous Arab woman had been delivered on August 8, 1952, of one of twins, and was brought to hospital in bad condition, with the second baby undelivered and an atonic uterus. She did not revive enough for delivery to be attempted, and died 21 hours after admission to hospital.

B. A primipara, aged 24 years, who was a native of Tunis, died on August 20, 1953. She had been delivered by forceps of a living child after two days' moderately severe labour. The fœtal head, which was in the occipito-posterior position, was manually rotated into an anterior position before delivery was achieved. She suffered a post-partum (intra-partum) hæmorrhage of considerable degree, and when her condition allowed, I performed a manual removal of the placenta from a relaxed uterus which contracted well afterwards. An episiotomy wound and a tear in the posterior vaginal wall were repaired under local anæsthesia. An hour later the patient was in satisfactory condition with a pulse rate of 72 per minute and no bleeding. After a further half hour the pulse rate had fallen to 64 per minute, the pulse was weak and the patient was restless, although there was no evidence of any bleeding and the uterus was contracted. Three-quarters of an hour later she collapsed, and all efforts at resuscitation failed. In the absence of an autopsy, for which permission was refused, the most likely diagnosis of pulmonary embolus could not be proved.

TABLE IV.
Tabulated Analysis of Fœtal Wastage.

Condition.	Total Number.	Primiparæ.	Multiparæ.
Prematurity	131	47	84
Major congenital abnormalities (stillbirths and neonatal deaths)	41	8	33
Maceration	49	10	39
Birth at home and dead on arrival	14	0	14

C. A multiparous woman, aged 23 years, who had been born in Egypt, died on July 17, 1954. She was six and a half months' pregnant when she was brought into hospital. She was in near shock with an accidental hæmorrhage after having received a blow on her abdomen. A hysterotomy was performed, and a dead fœtus showing hydrops fœtalis was extracted. On account of the patient's age and the fact that the uterus contracted reasonably well, hysterectomy was not carried out. The patient received a transfusion of 2800 ml. of blood in addition to saline and glucose solution, but bleeding continued. Her condition deteriorated progressively, and five hours later a hysterectomy was performed, followed by transfusion of another 1200 ml. of blood. Her condition at first improved very much after this, but she died on the third day after the operation from hepatic uræmia. We were unable to obtain enough Rh-negative blood, and she received several bottles of Rh-positive blood of her own group and also of group O.

D. An Israeli, aged 24 years, died on May 30, 1955. She had attended once at the ante-natal clinic in the fifth month of her fourth pregnancy. Two of the previous pregnancies had been terminated by artificial abortion. Some few hours after her admission to hospital in a state of jaundice she had a normal delivery, but her jaundice deepened, and a diagnosis of acute lymphocytic leukæmia was made. Three weeks after delivery she was transferred to the radiology department of Hadassah Hospital, Jerusalem, where she died four days later.

I have not stressed individual cases of interest or the highlights of the work.

One such was that of a Bedouin woman, who was delivered of one of a set of twins in her camp. About five hours later the arm of the second twin prolapsed, and she arrived in hospital after a further six hours with the mud-covered arm and umbilical cord protruding from the vagina. After some cleansing of the prolapsed parts internal version and extraction were performed, with manual removal of the placenta. The uterus contracted well, and with the help of antibiotics the mother made an uneventful recovery.

Another highlight was the successful replacement of an acutely inverted uterus. The woman was delivered at

home, and was brought to hospital some hours later with the inverted uterus prolapsed out of the vagina. She left hospital well after a week and has since then had a normal delivery in hospital.

When I was recounting some of these more spectacular and major interventions to an obstetrician in a country remote from here he commented: "God certainly lives in Israel."

I am prepared to admit that there has been very much good luck in the achievement of the recorded results, but also much work and many grey hairs have contributed.

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Reviews.

Clinical Gastroenterology. By F. Avery Jones, M.D. (Lond.), Hon. M.D. (Melbourne), F.R.C.P. (Lond.), and J. W. P. Gummer, M.S. (Lond.), F.R.C.S. (Eng.); 1960. Oxford: Blackwell Scientific Publications. 8¾" × 5¼", pp. 660, with illustrations. Price: 70s. (English).

AT last we have a first-class book on clinical gastroenterology, coming from the Gastro-Enterology Unit of the Central Middlesex Hospital, where Dr. Avery Jones has been responsible for lifting the standard in this branch of medicine to its present high level in the United Kingdom. The book is comprehensive, covering all aspects of gastroenterology apart from diseases of the liver. The authors hope it will be regarded as a companion volume to Professor Sheila Sherlock's "Diseases of the Liver and Biliary System".

The theme is decidedly clinical, with emphasis on diagnosis and management. The last mentioned is a fine blending of science and art, the best of the old and the new therapies. Opinion is fair and frank, with a wealth of experience clearly expressed; as an example, "kaolin, opium and codeine are the only drugs that give real assistance" in the general management of acute diarrhœa.

In the opening chapter, symptoms relating to alimentary tract disorders are discussed separately and very fully. This forms an introduction to gastro-enterology, and appropriately the next chapter deals with functional disorders. An up-to-date chapter on motility follows, and there are chapters on torsion and volvulus and on diverticulosis. Then come trauma, vascular disorders, tumours simple and malignant, and hiatus hernia, leading on to the common important diseases, notably peptic ulcer, steatorrhœa, alimentary tract hæmorrhage and ulcerative colitis. The book ends with an excellent description of diagnostic techniques.

This volume fulfils a need, and will prove invaluable to students, general practitioners and gastro-enterologists. It is worthwhile reading at all these levels, being practical, modern and authoritative. The presentation is excellent, logical and clear, detailed yet concise. The thread of continuity of thought and opinion by the two authors contrasts with the irregular views and standards in many multi-authored medical textbooks. Illustrations are profuse, mainly good X-ray pictures, tables and diagrams. There is one coloured plate of gastroscopy paintings which could well have been omitted, as it serves no useful purpose. Glossy paper is used throughout, the index is satisfactory, and references (not too many) are given at the end of each section.

We are delighted with this book, and recognize the industry and care that have gone into its production. There is no doubt that it will become the standard textbook in its field. Copies should be available in all Australian medical libraries, but most physicians will want it on their own shelves.

Discussions on Child Development. Edited by J. M. Tanner, M.D., D.Sc., D.P.M. and Barbel Ingelder; Volume IV, "The Proceedings of the Fourth Meeting of the World Health Organization Study Group on the Psychobiological Development of the Child, Geneva, 1956"; 1960. London: Tavistock Publications. 8¾" × 5¼", pp. 200. Price: 30s. (English).

THIS is the fourth and final volume of discussions on child development held annually from 1953 to 1956 by a group of experts under the ægis of the World Health Organization. The group covers a wide range of scientific disciplines — anthropology, psychology, psychoanalysis, electrophysiology, general systems theory and cybernetics.

The volume is divided into two parts, the first part being an essay by Professor Jean Piaget, of Geneva, on problems in child development, followed by comments on this from the group; the second part is an edited form of the actual group discussions, presided over by Dr. Fremont-Smith, of the Josiah Macy Foundation; in fact, this part closely resembles the form of the Macy Foundation reports.

The volume in both parts calls for deep concentration, and is by no means easy reading for those whose main interest in child development is at the clinical level. The subject is treated as an exercise in human biology, and much of the discussion is couched in the language of cybernetics. The editors warn prospective readers that an acquaintance with the earlier volumes would be an advantage, and note that they have "seen the growth of mutual comprehension amongst our Group", and how "remarks identical in content in the first and fourth Meetings were on the first occasion passed over in uncomprehending silence, and on the fourth handled easily and accurately as part of the common fund of knowledge". For the reader whose concentration may lapse, much of this volume also will be passed over in uncomprehending silence. The second part is more valuable as a demonstration of group dynamics than as a compendium on child development, and one is left with the feeling that for some members of the group the child is a convenient locus from which to embark upon an intellectual exercise. Others in the group apply themselves to the subject matter in more specific fashion. For the unwary, this book may prove to be a disappointment. For those who have followed and enjoyed the previous volumes, it will be a delight.

The Year Book of Neurology, Psychiatry and Neurosurgery (1959-1960 Year Book Series). "Neurology" edited by Roland P. Mackay, M.D., "Psychiatry" edited by S. Bernard Wortis, M.D., "Neurosurgery" edited by Oscar Sugar, M.D.; 1960. Chicago: The Year Book Publishers. Melbourne: Ramsay's Medical Books. 7¼" × 5", pp. 640 with many illustrations. Price: £4 19s.

THIS Year Book is divided into the usual three sections, under the same respective editors. In the introduction to the section on neurology, R. P. Mackay takes the opportunity to scan the major accomplishments in his subject during the preceding decade. He states that among basic neurological disciplines, neuroanatomy and neurophysiology, now firmly wedded, occupy the chief position, and notes some of the tremendous advances which have occurred in this field. Other outstanding advances are noted under the headings of virus diseases, convulsive disorders, degenerative diseases, vascular disorders and therapeutic measures. The abstracts in this section are arranged in the usual chapters, a change from the previous year being the allotment of separate sub-chapters to the cerebral palsies of childhood and to myasthenia gravis.

In his introduction to the section on psychiatry, S. B. Wortis touches briefly on what appear to be the significant

advances of the year, and gives an extensive list of "some interesting books in the field" published during the year, together with a list of some special symposia, one of "special articles worth reading" and one of "some psychopharmacologic articles worth reading". This is a usual feature of this section, and, in conjunction with the abstracts in the succeeding pages, provides a convenient means of quick reference to the titles of the main contributions on the subject during the period under review.

The abstracts of the third section, on neurosurgery, are divided into chapters on anatomy and physiology, diagnosis, technical notes, congenital disorders, infections, trauma, disk disease, vascular disease (subdivided into obstructive lesions and hæmorrhages), tumours, pain problems, stereotaxic surgery and epilepsy, with frequent editorial comments.

These three sections provide very adequate coverage of the work published during the year under review in the three major subjects which together make up the medicine of the nervous system.

The Urological Aspects of Bilharziasis in Rhodesia. By R. M. Honey, M.B., F.R.C.S. (Edin.), and M. Gelfand, C.B.E., M.D., F.R.C.P.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" x 5½", pp. 80, with illustrations. Price: 7s. 6d. net. (English.)

TEN years ago it was stated at the first international meeting of the WHO/OIHP Group on Bilharziasis that the state of knowledge of this disease at that time was comparable with that of malaria at the beginning of the century. From the records of 300 European and 100 African patients with urinary bilharziasis, the authors have compiled a careful study of the disease, laying special emphasis on the late results. Twenty years ago, they state, the disease was regarded as benign, causing vague ill-health and occasionally ureteric stricture. This study shows that the ureteric stricture is only one facet of the picture, and that bladder damage, hydronephrosis and other lesions can occur in the absence of stricture.

Differences in the manifestations of the disease in African and European patients are ascribed to the earlier treatment of the Europeans, who are usually first encountered in the acute phase. Many recent techniques of dealing with the late results are discussed, such as ileo-cystoplasty, to enlarge a fibrotic contracted bladder. The tendency of the late manifestations to occur in young people is stressed.

Many intravenous and retrograde pyelograms illustrate the living pathology of urinary bilharziasis in a study which is the result of 20 years of work in a heavily infested area.

Principles of Medicine: An Integrated Textbook for Nurses. By James Verney Cable, M.D., M.R.C.P., F.R.A.C.P., with a foreword by Miss Flora Cameron, O.B.E., R.N., R.M.; 1960. Christchurch: N. M. Peryer Limited. 8½" x 5½", pp. 674, with 129 illustrations. Price: 55s. (New Zealand).

THE author of this book has produced the answer to a lecturer's prayer. Although it has a distinct flavouring of what one might term colonialism, the book could be lifted out of its New Zealand habitat and applied anywhere in the British Commonwealth.

The format is clear and the style concise. Dr. Cable is obviously in touch with modern medicine, and his review on antibiotic drug therapy is particularly up to date. Chapter by chapter he highlights disease entities well, and throughout the book the text is profusely illustrated. The diagrams are both accurate and instructive. Introductory anatomy and physiology make for easier understanding of the subsequent text.

The chapter on congestive cardiac failure is a masterpiece of simplicity; it contains the essentials of modern theories on œdema and the anti-diuretic hormone.

We were mildly surprised with the statement that nothing can be done for paralysis agitans. We should have thought that stereotactic encephalotomy for diseases of the basal ganglia was sufficiently well known now to be included in the textbooks. However, in the main we have nothing but praise for Dr. Cable's textbook.

Diseases of the Nails. By V. Pardo-Castello, M.D., and Osvaldo A. Pardo, M.D.; third edition: 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 8½" x 5½", pp. 312, with illustrations. Price: 68s. (English).

THIS third edition is a worthy successor to the first and second editions, produced in 1936 and 1941 respectively. It is the main authoritative work in English on the subject of diseases of the nails, and constitutes virtually a monograph with 113 excellent illustrations in black and white. These are indexed in the front of the volume after the list of contents.

The 462 references occupy pages 246 to 277, and are followed by the index at the end of the volume. The quality of type and paper is as good as ever, and the text is eminently readable, providing a useful and reliable reference, as far as any book can be reliable which deals with the multitude of minute changes in the nails affected by local and systemic disease. Up-to-date information is critically sifted, and includes extensive references to the use of griseofulvin in onychomycosis, the changes produced in the nails by various occupational processes, etc.

Apart from its appeal to dermatologists generally, this work is an essential part of the library of the dermatologist-teacher. All concerned with undergraduate and post-graduate instruction in dermatology should read and refer to this book.

The Year Book of Cancer, 1959-1960 Year Book Series. Compiled and edited by Randolph Lee Clark, Jnr, B.S., M.D., M.Sc., D.Sc., and Russell W. Cumley, B.A., M.A., Ph.D., 1960. Chicago: The Year Book Publishers Inc. 7½" x 5", pp. 534, with many illustrations. Price: £4 13s. 6d.

THIS important member of the Year Book Series again brings us a representative collection of abstracts of important papers concerned with diagnostic, therapeutic and basic studies relating to cancer which have appeared during the year under review. With the assistance of the 470 members of their editorial board, the editors are enabled to present a comprehensive review of this very wide field, and in the collection of their material they have endeavoured to reflect shifts of emphasis in current cancer research. In their attempt to compress the best of the literature of the year into one easy-to-use volume, the editors have largely avoided the controversial subject, the incomplete investigation and the undocumented work. One exception to the elimination of controversial material is the inclusion of a review of a series of articles by Sir Ronald Fisher on his currently favoured topic. A special feature is an article on the TNM system of staging, written for the Year Book by M. S. Copeland. This system is an attempt to set up a workable method for the clinical classification of cancers of various types according to a uniform system of general application. This system has been worked out by the Clinical Classification Committee of the U.I.C.C. (International Union against Cancer), and is at present on trial at various centres.

Altogether, the editors are to be congratulated on having again produced a volume which is both highly readable and packed with current information about the results of cancer research in its many aspects.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Handbook of Physiology: Section 1, Neurophysiology", edited by John Field; Volume III, 1960. Washington: American Physiological Society; Baltimore: The Williams & Wilkins Company. 11" x 8½", pp. 1441-2013, with illustrations. Price £11.

"Tobacco, Experimental and Clinical Studies: A Comprehensive Account of the World Literature", by P. S. Larson, Ph.D., H. B. Haag, M.D., and H. Silvette, Ph.D.; 1961. Baltimore: The Williams & Wilkins Company. 11" x 8½", pp. 944. Price: £11.

"Parasitology (Protozoology and Helminthology) in Relation to Clinical Medicine", by K. D. Chatterjee, M.D. (Calcutta); Third Edition; 1960. Calcutta: K. D. Chatterjee. 9¾" x 6¾", pp. 200, with 128 illustrations, including 26 coloured plates. Price: Rs. 18.75 (India).

"Pædiatrics for the Practitioner: Supplement 1960", edited by Wilfrid Gaisford, M.D., M.Sc., F.R.C.P., and Reginald Lightwood, M.D., F.R.C.P., D.P.H.; 1960. London: Butterworth & Co. (Publishers) Ltd. 9¾" x 6½", pp. 164, with illustrations. Price: Not stated.

"Radiation Therapy of Early Prostatic Cancer", by R. H. Flocks, M.D., and D. A. Culp, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" x 6", pp. 86, with illustrations. Price: 36s. (English).

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SATURDAY, MARCH 18, 1961.

THE EPIDEMIOLOGY OF CAT-SCRATCH DISEASE.

AMONG the prolific crop of new diseases which have sprung up within the professional life-time of many of us, cat-scratch disease has a distinctively individualistic quality appropriate to its name. Its association with the symbol of domesticity gives it an intimate air; it is undoubtedly caused by an infective agent, but the causative organism still eludes discovery; it is rare, but probably not so rare that any general practitioner may not expect to encounter it at some time during his professional life if he is sufficiently on the alert; it is ordinarily a fairly benign condition, which undoubtedly causes it frequently to be overlooked. In about 90% of cases there is a history of close contact with a cat, and very frequently of a cat scratch or bite, and there seems no reason to doubt that the cat is the usual source of the infection. However, as the causative organism has not been identified, and there is no evidence that it causes any recognizable illness in cats, the natural history of the disease outside man is quite unknown. As material from affected glands is invariably sterile on attempted culture, it is a reasonable assumption that cat-scratch disease is caused by a virus. Early in the history of the disease, in 1951, P. Mollaret suggested that this was a virus of the lymphogranuloma-psittacosis group, and this suggestion has been repeated by some subsequent investigators. However, Sir Samuel Bedson, who presented a comprehensive survey of this group in the Harben Lectures for 1958,[1] regarded this conclusion as very doubtful.

In these circumstances, three papers by W. J. Warwick and R. A. Good[2] on an epidemic of cat-scratch disease in the twin cities of Minneapolis and St. Paul make an interesting contribution to the subject. In December, 1955, these authors became aware of the occurrence of an unusual number of cases of the condition, and they then launched a publicity campaign in the Twin Cities in an effort to trace the full extent of the epidemic. The harvest was not abundant, for in two years they managed to trace 18 established cases, but careful analysis produced some interesting information. In the first place, the onset of lymphadenopathy in all cases occurred between September and February, the majority of cases being concentrated in the three months, November, December and January. When Warwick and Good turned to the literature, they found only two previously recorded epidemics, but a consideration of other published reports made it clear that there had been other unrecognized epidemics. Further, all these "chronological concentrations" of cases of cat-scratch fever occurred during the autumn and winter months. An analysis of 139 case reports from Canada and the United States, in which sufficient information was given, showed that while sporadic cases might occur at any time of the year, 40% occurred in November or December, and 90% between September 1 and the end of February.

A second interesting point in the Minnesota epidemic was that of the 18 cases, 10 occurred in four families. In all but two cases of the series, the patients had had prolonged contact with a "family" cat. In eight families the entire family was studied by means of skin testing, and in six of these one or more additional members of the family gave a positive reaction to a skin test with cat-scratch disease antigen. It was noticeable that it was those members of the family who had most to do with the cat who developed positive skin reactions—for example, in one family of 10, two children were devoted to the kitten and both acquired cat-scratch disease; the other six children shunned the kitten in favour of the puppy and were not affected. Warwick and Good note that there is much variation in the interval between cases in the same family. They quote one case from the literature in which husband and wife developed the disease 12 months apart, apparently having both acquired it from the same cat. However, the available evidence indicates that it is commoner for cases in family epidemics to be concentrated into a short period of time. Warwick and Good note that a cat has been a member of all families in which epidemics of cat-scratch disease have appeared.

A third point brought out in the Minnesota epidemic was that all the cats concerned were in fact kittens, all being less than six months old. French authors, who have contributed largely to the literature on this disease, have also noted that cats which spread cat-scratch fever are always young and playful. Many authors pay no attention to this point, but Warwick and Good have found reports of one or two cases in which it is stated that the cat was old. They suggest that the implication mainly of young cats may be explicable by the fact that these are more cuddly and so are more likely to be handled, and that they are more prone to scratch unintentionally than older cats. However, it seems equally possible that this observation may have some bearing on the epidemiology of the virus in the cat population. Psittacosis in parrots is normally acquired in the nest, and the infection tends to die out as the birds grow older.

Warwick and Good's third paper is a discussion of the intradermal skin test with cat-scratch disease antigen, which they regard as the test on which a positive diagnosis

[1] *J. roy. Inst. publ. Hlth*, 1959, 22: 99 (April).
[2] *Amer. J. Dis. Child.*, 1960, 100: 228 (August).

primarily depends, and of the results of surveys carried out by this means. Their publicity campaign gave them the opportunity of skin-testing a large number of families in which a case of cat-scratch disease had been suspected, but in which some alternative diagnosis was eventually established. In this way, they tested 206 subjects unconnected with cases of cat-scratch disease and found an incidence of 5·8% of positive reactions, as compared with 26% in the families of patients in whom the disease had been recognized. Other smaller series published elsewhere show results varying from zero to 7·5%, so it seems reasonable to accept 5% as the incidence of positive reactors (and, by inference, of those who have had subclinical or unrecognized infections) in the general population of North American cities.

Whether the North American pattern of small winter epidemics of the disease will be found elsewhere is, of course, not certain. Cat-scratch fever is of world-wide distribution, but in Australia, while cases are seen not infrequently, there are few published reports of the condition. In reporting three cases from Western Australia, the first to be recorded from that State, J. H. R. Watson[3] refers to the time of year at which the illness occurred in only one case—that was in July. In the few cases mentioned in reports of clinical meetings details are usually scanty, in some cases inadequate even to explain the grounds for the diagnosis. In New Zealand, J. D. Reid[4] has reported on 40 cases in which a positive result to an intradermal test was obtained, out of 116 cases of regional lymphadenitis and other illnesses investigated over a period of less than three years. An interesting finding was that nine of the 40 patients with a positive reaction to the skin test had positive results of complement fixation tests to a psittacosis antigen, with titres greater than 1:5; of 53 patients with negative results of the skin test, only one showed a positive result when tests with psittacosis antigen were performed. There would seem to be an opportunity here, for someone in a position to collect a series of cases, to undertake a profitable investigation into the epidemiology of the condition in Australia. It is perhaps a case in which the fact-finding potentiatities of the Australian College of General Practitioners might be usefully enlisted. The disease may not be of great importance, but it represents a gap in our knowledge which presents a challenge to the epidemiologist (that is to say, anyone interested in the natural history of diseases), and the filling of any gap helps to complete the over-all panorama of human pathology, and thereby assists in the understanding of the whole.

[3] MED. J. AUST., 1956, 2: 20 (July 7).
[4] *N.Z. med. J.*, 1959, 58: 39 (February).

Current Comment.

BLOOD PICTURES OF AUSTRALIAN NATIVE ANIMALS.

CONSIDERABLE gaps still exist in our knowledge of the physiology of the Australian native animals, but recently the hitherto unknown blood pictures of a monotreme, the echidna or Australian spiny ant-eater (*Tachyglossus aculeatus*), and of a eucalyptus leaf eating marsupial, the koala (*Phascolarctos cinereus*), have been studied by A. Bolliger and T. C. Backhouse.[1]

The only two existing monotremes, the echidna and the platypus, forming the allegedly lowest order of the mammalian class and referred to as prototheria, have definite similarities to the reptiles, e.g., in their skeletal peculiarities and their egg-laying habits. They are further remarkable for their geological antiquity and may be considered as living fossils, since no evidence is available for a gradual process of monotreme evolution. An analysis of the monotreme blood picture seemed therefore desirable, and blood counts were performed on some 40 echidnas.

Two problems were of particular interest. The first was whether the blood picture of the echidna showed any similarities to that of reptiles. The latter is characterized by oval nucleated erythrocytes and a considerable variety of forms of leucocytes, which frequently include large numbers of basophils and eosinophils with round, elliptical and rod-like granules. The second problem was what were the characteristics of the monotreme blood picture, which in all probability has remained unchanged for nearly 200 million years. Relating to both these problems, the normal blood picture of the echidna was found to be similar to that of the present-day higher mammals or eutheria (which also include man). It exhibited no reptilian characteristics, and, in all normal instances, the red corpuscles were non-nucleated, non-reticulated, biconcave circular discs. The leucocytes were identical with those seen in advanced mammals, the only qualification being a definite tendency to remain simple by human haematological standards. Neutrophils and lymphocytes were always of mature form, and comparatively few monocytes could be seen. Eosinophils were only few in numbers and of the type seen in mammalian blood, and basophils were practically absent. These findings seem to indicate that the blood picture of the echidna represents the basic pattern which applies to all mammals. This picture was already in existence some 200 million years ago as the monotremes diverged from the main mammalian line of evolution.

From the evolutionary aspects, marsupials (metatheria) are considered to be closer to higher mammals than the monotremes. In the koala, for instance, the normal blood picture is related to that of the echidna, but it is more complex than that of the latter. Nucleated red cells and reticulocytes were always present, and monocytes occurred in considerable numbers. Hæmoglobin values were low compared with either man or echidna. In the absence of investigations on other large groups of marsupials it is impossible to consider these findings as typical of the marsupials as a whole. In this context it may be pointed out that the koala lives exclusively on eucalyptus leaves, a diet which would be toxic to most mammals. These leaves contain as much as 5% of essential oils, of which cineol is the most common. One may therefore wonder if the permanent intake of potentially toxic substances has an influence on the blood picture. This is difficult to decide. In the koala, however, two cases of primary blood disease were in evidence, a lymphogenous leukæmia and a hæmolytic process. The former was observed on a dead specimen, and the latter was under observation for seven months. All attempts to correct this anæmia by the administration of iron, vitamin B_{12}, folic acid and liver extract were unsuccessful, and the animal died. This anæmia did not duplicate completely any human form of hæmolytic anæmia (T. C. Backhouse and A. Bolliger[2]). One might speculate that these blood diseases were somehow connected with the diet of the koala. No primary

[1] *Proc. Zool. Soc. Lond.*, 1960, 135: 91; *Aust. J. Zool.*, 1960, 8: 363.
[2] *Aust. J. Zool.*, 1961, in the press.

blood disease was observed in the echidna. This may be suggestive, but in such a small series no definite conclusions can be drawn from this latter fact.

BILHARZIASIS CONTROL IN THE PHILIPPINES.

SCHISTOSOMIASIS (bilharziasis) is fortunately not endemic in Australia, but the disease, in one or other of its three forms, is of great medical and economic importance over large parts of the tropical and subtropical regions, and ranks with malaria, hookworm and filariasis as one of the great parasitic scourges of the world. It is prevalent in many parts of South-East Asia and of the adjacent islands. It will be recalled that the intermediate host of the parasite is a small water snail, from which are liberated the cercariæ; these are capable of penetrating the skin of their mammalian hosts, which include man, and so find their way into the circulation and ultimately to the portal venous system. The disease is therefore characteristically a disease of rice-growing areas and places where irrigation involves working in the water; in affected regions it is a problem to be considered whenever new areas are brought under irrigation.

It is estimated that 300,000 Filipinos are afflicted with the disease, and this is an area where important work has been carried out on ways and means of eradicating the disease, with the active help of the World Health Organization. Control of the disease involves education of the rural population in the necessity of proper sanitation on the one hand and, on the other, attempts to eliminate the intermediate host. An important step forward has been the demonstration that the responsible water snails can be eliminated by methods which will also increase the productivity of the land. Experiments have shown that drainage of swamps and the clearing of vegetation from the canals will result in disappearance of the water snails. The same result was achieved by improved cultivation of the rice fields; in fields which were carefully ploughed and weeded and in which the rice seedlings were planted in straight rows at measured distances, the water snails were eliminated and the harvest was increased threefold. In water-logged areas incapable of drainage the snails can be kept down by the digging of ponds for fish farming. The eradication of individual helminth infections by drugs is of course possible, and this line of attack is also being studied, but in the face of a problem of such vast proportions it is likely to remain secondary to the attack on the infection at its source.

The problem of enlisting the cooperation of large underprivileged rural populations and of persuading them to keep their ditches and fields clear of weeds, and to adopt modern standards of sanitation, is no doubt a formidable one, but in the Philippines the extent of the problem can at least be clearly defined, thanks to surveys carried out by the Philippine Department of Health and by World Health Organization experts. WHO has already provided considerable assistance in both personnel and equipment; with further assistance from the same source and from the Food and Agriculture Organization of the United Nations, the Philippine health authorities have at least a reasonable hope of eventually gaining the upper hand over schistosomiasis, and thereby giving a lead to other areas where the disease is still rampant.

ACID AND ALKALINE PHOSPHATASE IN NORMAL AND ABNORMAL PROSTATIC TISSUE.

SINCE it was first shown in 1936 that there is an elevation of serum acid phosphatase activity in patients with metastatic cancer of the prostate, the measurement of this activity (expressed as Bodansky units or King-Armstrong units, according to the method employed) has become a standard part of the clinical investigation of patients with this condition. In a recent paper presenting a clinical and histochemical study of acid and alkaline phosphatase in normal and abnormal prostatic tissue, J. B. Goetsch[1] discusses the significance of the variations in level of activity commonly found. He points out that the degree of elevation of serum acid phosphatase activity in cases of prostatic cancer is highly variable, and does not always parallel the extent of demonstrable metastatic disease. Patients may even be found who have widespread metastases, but whose serum acid phosphatase activity is within normal limits. Goetsch's study was undertaken with the object of elucidating such discrepancies. It was thought that a cytological study of the intracellular acid phosphatase enzyme distribution in normal persons, in those with benign hyperplasia and, finally, in those with prostatic carcinoma would lead to a better understanding of this problem, especially if the results were correlated with the clinical picture. The material studied consisted of 24 cases of benign hyperplasia, 54 cases of prostatic carcinoma and two normal glands from young adults who had died suddenly of causes not associated with previous ill-health.

From the study it appears that a high degree of acid phosphatase activity is always found in prostatic epithelial cells, either benign or malignant. The activity is greatest in the secreting end of the cell. In carcinoma there is no difference between the primary lesion and its metastases. Prostatic cells differ from other cells containing acid phosphatase in that the prostate manufactures this enzyme as a secretory product. This characteristic is retained by the cells of prostatic carcinoma, but varies from one carcinoma to another and even among cells of the same neoplasm. Goetsch finds that there is no correlation between the acid phosphatase activity of the cell cytoplasm and the morphology of the carcinoma, the malignant characteristics of the cells, or the level of acid phosphatase in the blood serum. In the normal prostate, the acid phosphatase is formed as a part of the prostatic secretion and never enters the general body fluids, since it is a purely external secretion like milk or sweat. However, prostatic cancer has no drainage duct system, and as a consequence the secretion produced becomes part of the general body fluids. It is apparent that in cancer of the prostate the level of serum acid phosphatase activity is determined on the one hand by the amount of prostatic epithelium that exists apart from the normal drainage duct system of the prostate, and on the other by the rate at which the enzyme is being manufactured and secreted from the cell. Goetsch considers that the latter seems to be the important factor. Since it was observed that the intracellular enzyme distribution was essentially unchanged after castration or after œstrogen therapy, he concludes that such measures have no direct effect on the enzyme, but rather that, as a part of a general lowering of cell metabolism, there is a lowering of the rate of acid phosphatase production.

Another interesting observation concerns the problem of why prostatic carcinoma usually produces osteoplastic metastases, unlike almost all other neoplasms except an occasional breast cancer. Goetsch states that there is evidence to show that such bone lesions must be associated with the presence of a high local concentration of enzyme. He therefore suggests that under conditions of a high level of acid phosphatase activity in fluid surrounding bone trabeculæ, phosphate radicals are liberated from material in solution, phosphate salts are formed, and these are utilized in the calcification of bony matrix at a higher rate than in the surrounding normal bone. Goetsch points out that such bone lesions are not always associated with a high circulating blood serum level of acid phosphatase, but that it is rather a matter of the presence or absence of a high level of acid phosphatase enzyme activity at the site of the metastasis. Whether the level of enzyme activity in the general body fluids is elevated or not depends on the rate of production of enzyme by the entire cancer and the rate of excretion of the enzyme by the body of the host.

[1] *J. Urol. (Baltimore)*, 1960, 84: 636 (November).

Abstracts from Medical Literature.

NEUROLOGY.

Constructional Apraxia with Unilateral Cerebral Lesions.

M. PIERCY *et alii* (*Brain*, June, 1960) compare constructional apraxia associated with unilateral cerebral lesions on the right and left sides. They have analysed 67 cases in patients with unilateral lesions seen by them in eight years. Their observations are that the disability is more frequent and more severe in right hemisphere cases and that the localization of responsible lesions tends to be more restricted in right hemisphere cases. Qualitative differences between the constructional performances in left and right hemisphere cases are analysed and the authors conclude that the differences between the two groups in the severity and frequency of the disability cannot be accounted for by the masking effect of paresis and dysphasia or by unilateral imperception. Also the qualitative differences observed cannot be attributed to differences in severity alone.

Visual-Constructive Disabilities with Left Cerebral Hemisphere Lesions.

J. MCFIE AND O. L. ZANGWILL (*Brain*, June, 1960) discuss a group of eight patients in whom lesions in the left cerebral hemisphere were accompanied by a marked degree of visual-constructive disability. They found that, in contrast to previously described groups with right-sided lesions, the disability in this group was rarely associated with unilateral neglect, apraxia for dressing, or failure on tests involving spatial analysis, including topographical memory, but that it was frequently associated with right-left disorientation and general intellectual impairment, including failure on sorting tests, with which the groups with right-sided lesions had little difficulty. There are also qualitative differences in the nature of the visual-constructive breakdown between the groups with left-sided and right-sided lesions, the former showing more difficulty in manipulation and restriction of response. It is suggested that the disability shown by the present group of patients corresponds to the classical description of constructional apraxia, and is essentially different from the disability associated with spatial agnosia found with right-sided lesions. It is noted that the lesions in all cases were in the posterior parietal region, and it is suggested that fuller analysis of the disability will depend upon examination of series of patients with adequately localized lesions.

Intermediate Carbohydrate Metabolism in Multiple Sclerosis.

B. MCARDLE *et alii* (*J. Neurol., Neurosurg. Psychiat.*, May, 1960), in their studies on intermediate carbohydrate metabolism in multiple sclerosis, have found that in seven out of 20 cases of multiple sclerosis the level of pyruvate rose above normal after the ingestion of glucose. This was determined by a chromatographic method. In these seven cases there were also an abnormal rise in α-ketoglutarate after the ingestion of glucose and low fasting plasma citrate levels. The resting blood level of α-ketoglutarate was higher in females than in males. The pyruvate level in the cerebro-spinal fluid was normal in 12 patients with multiple sclerosis. The abnormalities of pyruvate metabolism were more closely correlated with complications such as spasticity and malnutrition than with activity. It is concluded that a disturbance of pyruvate metabolism is unlikely to be causally related to the disease.

Serum Potassium Levels and Myotonia.

P. LAYBURN AND J. WALTON (*J. Neurol., Neurosurg. Psychiat.*, May, 1960) discuss the effect of changes in serum potassium levels upon myotonia. Five patients with dystrophia myotonica and two with myotonia congenita received a potassium-binding ion-exchange resin by mouth for from 15 to 24 days. During treatment the serum potassium level and the duration of the myotonic after-contraction were measured daily. In three cases there was no consistent fall in the serum potassium level and no reduction in the myotonia. A progressive reduction of serum potassium level was achieved in four cases and in three this produced slight objective decrease in the myotonia, but only in one case was it convincing. No patient obtained subjective benefit from the treatment. It is concluded that potassium-absorbing ion-exchange resins are of no practical value in the treatment of myotonia.

Focal Cortical Cerebellar Sclerosis.

L. C. MCHENRY, JR, *et alii* (*Arch. Neurol.*, July, 1960) describe four cases of cerebellar sclerosis involving chiefly the superior and inferior semi-lunar lobules, and without apparent symptoms of cerebellar disease. They state that focal cortical cerebellar sclerosis can be differentiated from other cerebellar lesions by its characteristic histology. They found that the lesions in the adult are of long standing, and there is no reason to believe that there was continuing activity in any of the reported cases. The absence of gross cerebellar symptoms and signs is probably explained by the capacity of the nervous system to adapt itself to cerebellar cortical lesions of long standing as is well known in the cases of cerebellar hypoplasia. The cause of the lesion is not demonstrable from the histology. The authors stress the participation of the leptomeninges in this lesion. However, evidence is lacking of any definite or primary extraparenchymatous causative factor.

Nerve Block Distal to a Lesion.

R. F. KIBLER AND P. W. NATHAN (*J. Neurol., Neurosurg. Psychiat.*, May, 1960) discuss the relief of pain and paræsthesiæ by nerve block distal to a lesion. They point out that lesions of afferent pathways may give rise to a variety of spontaneous sensations. When a lesion affects nerves, nerve roots, the root entry zone, or the spino-thalamic tract, the sensations are usually those of pain and painful pins and needles; when it affects the posterior columns the sensation is one of painless pins and needles or of tingling. They suggest that the pain and paræsthesiæ are due to discharge of nerve fibres in or near the lesion, and that the lesion or the afferent pathway causes these nerve fibres to fire off. They present evidence that local anæsthetic injection of the afferent pathway, distal to the site of the lesion, may stop the pain or paræsthesiæ; further, that this effect may outlast the duration of the anæsthesia; and that blocking a peripheral nerve supplying a large part but not the whole of the region where the pain or paræsthesiæ are felt may remove these sensations from the entire region. Among the eight cases investigated were examples of disseminated sclerosis, syringomyelia, and intramedullary spinal cord lesion. The authors conclude from their investigations that blocking an afferent pathway at a point distal to the site of a lesion stops the spontaneous sensations which result from the lesion. The pain and paræsthesiæ probably are due to impulses arriving from the periphery, which are somehow altered by the lesion.

Metachromatic Leuco-Encephalopathy: A Form of Lipidosis.

R. M. NORMAN *et alii* (*Brain*, September, 1960) discuss a late infantile form of metachromatic leuco-encephalopathy which was delineated by Brain and Greenfield in 1950 and is a form of lipidosis. The present authors have studied two familial cases of the disorder from the clinical, histological and chemical points of view. The recent discovery that the brain and kidney in this condition contain a large excess of sulphatide has been confirmed. The presence of this substance accounts for metachromatic staining of the lipid found in the degenerating white matter, in the peripheral nerves, in certain groups of nerve cells and in the epithelium of the renal tubules and intrahepatic bile ducts. Sulphatide is not the only product of the metabolic disturbance present in this disease, for after removal of metachromatic lipid by solvents much granular material staining roughly by the periodic acid Schiff method remains in the tissues. The cases described were remarkable for the selective involvement of the nerve cells of many of the brain-stem nuclei in the process of lipid storage. The severe destruction of the nerve cells occurred in the globus pallidus, subthalamic nucleus and claustrum, and in one case there was diffuse atrophy of the granular layer of the cerebellum. It is suggested that this degenerative process is the result of a lethal intracellular metabolic defect and that the striking disappearance of interfascicular oligodendroglia in this disease may be due to a similar cause.

Cutaneous Reflex Changes in Development and Aging.

J. W. MAGLADERY *et alii* (*Arch. Neurol.*, July, 1960) have studied electromyographically the cutaneous reflexes, namely plantar and abdominal responses, in normal subjects from infancy to old age. They found that, with the type of stimulation usually employed clinically, latencies were considerably greater in both the

very young and the elderly than in young adults. When intense electrical stimuli were used, all latent periods were materially shorter. They did not differ significantly between older persons and young adults, although latencies in childhood were longer. Simple tactile reaction times, though increased in children, were little altered in the elderly. The authors discuss possible implications of these latency differences in a consideration of mechanisms underlying motor activity in maturation and aging. They suggest that regressive changes or immaturity at the periphery cannot be held responsible for long latencies of clinical reflex responses, either in the elderly or in childhood. They suggest an alteration in some central mechanism such as diminished excitatory influence from higher levels. This would be an acceptable interpretation in the elderly and in childhood, particularly as the prolonged abdominal reflex latencies of childhood and of advanced years resemble those described in the presence of relatively minimal cerebral lesions.

Congenital Universal Insensitivity to Pain.

D. W. BAXTER AND J. OLSZEWSKI (*Brain*, September, 1960) discuss congenital universal insensitivity to pain. They report the clinical findings and post-mortem results in a patient who had been followed for several years. Such patients fail to appreciate pain, but can distinguish between sharp and dull, and warm and cold. The sensation of tickle is also absent. In the authors' case, the corneal reflexes were diminished, nose tickle was absent, the gag reflex was diminished, the patient had brisk deep reflexes and the plantar reflexes were flexor. Touch, vibration sense and joint sense were normal. During the course of the follow-up of this patient, X-ray examinations of the spinal cord showed changes in the vertebræ, some of which were partially destroyed, and later the patient showed loss of substance of the femoral head. The importance of the loss of pain sensation as the ætiological factor producing neuropathic joint disease is discussed. The post-mortem examination in this case failed to demonstrate any abnormality of those parts of the nervous system thought to be concerned with the transmission, elaboration and perception of pain. The authors ask whether there is a defect in terms of organization rather than in structure and discuss possible perceptual or psychological variations that might produce the syndrome.

PSYCHIATRY.

The Psychotherapist's Contribution to the Treatment Process.

H. H. STRUPP (*Arch. gen. Psychiat.*, September, 1960) discusses the nature of the psychotherapist's contribution to the treatment process and asserts his belief that the greatest technical skill offers no substitute for the preeminent need for integrity, honesty and dedication on the part of the psychotherapist. Unless these are at the core of the therapist's personality he will not be successful in helping the patient to develop them within himself. The author comments on Freudian concepts of counter-transference which do not provide for positive influences which may have a beneficial effect. He summarizes the evidence he has obtained on the influence of the therapist's personality and attitude on the patient and the therapeutic relationship. All the evidence is indirect, and only presumptive, but has been confirmed by informal observations made at diagnostic conferences and the like. He has demonstrated that experienced therapists ask fewer exploratory questions and that their communications are more inferential. In another study, a sound film of an initial interview, with 28 interruptions, was shown to some 200 psychiatrists. At each interruption they wrote down what they would do; subsequently they completed a comprehensive questionnaire on diagnostic impressions, treatment plans, goals, etc. The results showed an interaction between the clinical observations of the therapist, the nature of the treatment recommendations, and his attitude towards the patient, and these in turn exerted an effect on the manner of his communications. Other studies, which led to similar conclusions, are briefly summarized.

The Doctor in the Treatment of Schizophrenia.

J. C. WHITEHORN AND B. BETZ (*Amer. J. Psychiat.*, September, 1960) state that recent studies have focused attention on the personal characteristics of those physicians who have a high proportion of improvement in their schizophrenic patients, as contrasted with those who have a relatively low proportion of improvement. They discuss two groups of psychiatrists, the first (Group A) consisting of seven who had treated 48 patients with an improvement rate of 75%, the second (Group B) consisting of seven who had treated 52 patients with an improvement rate of 27%. With other classifications of disease both groups did equally well. Much of schizophrenic behaviour and attitudes seems to be a direct expression of a special orientation towards authority, external or imposed. Such expression is evident in the classical experience of being controlled or influenced. The schizophrenic patient does not live by give-and-take methods and tends to avoid being involved with others. The authors suggest that the approach of Group A is problem-solving, and not coercive, an approach which seems more acceptable to the resentful boxed-in patient. The members of this group also reveal a capacity to be perceptive of the individualistic inner experiences of the patient, and any solutions to the patient's problems are worked out through collaborative exploration rather than in the mode of authoritative instruction. The doctors of Group B were rather rigid in their attitudes, had mechanically-inclined interests, and were orientated towards precision and a rule-of-thumb approach; these attitudes probably constituted a hindrance to the development of self-trust and social spontaneity in the schizophrenic patient. The authors conclude that some shifting from the rigid to the more accommodating approach appears to be possible, and does improve the therapeutic effectiveness of the physician with his schizophrenic patients.

Aggression and Forbiddenness in Voyeurism.

I. D. YALOM (*Arch. gen. Psychiat.*, September, 1960) comments on the vagueness of the term voyeurism, and on the fact that very few voyeurs come to medical attention. He outlines the case histories of eight patients, whom he refers to as "offensive voyeurs", and defines them as having an exaggerated desire to see, by stealth, a member of the opposite sex either in some stage of undress, in the sexual act, or in the act of excretion, which is so intense that it surpasses in importance the normal sexual act. A regularly appearing phenomenon in these patients and an indispensable ingredient for their gratification is the doing of that which is prohibited. The author comments on the obvious similarity between the voyeur's sexual search in the realm of the forbidden and the child's sexual curiosity which is met by silence and evasion, cloaking sex with an enticing aura of forbiddenness. Sadistic features were especially apparent in the cases studied; attempted rape, assault, arson and major burglary occurred when the urge to peep was frustrated. The author comments on the psychopathology, and gives the analytic interpretation that the patients are fixated on scenes which have aroused castration anxiety and attempt to deny the justification of their fright by repetitive reviewing of the frightening scene. Another possible factor, he considers, is the frank sexual pleasure experienced by identification with one of the persons in the sexual act witnessed.

Modes of Abstract Thinking and Psychosis.

N. MCCONAGHY (*Amer. J. Psychiat.*, August, 1960) suggests that there is a wide difference in the modes of thinking between schizophrenia proper and paranoid states. "Loosening of the associational structure" was one of the primary symptoms of schizophrenia as described originally by Bleuler. This has been alternatively described as "a weakness of inhibition of thoughts", so that irrelevant, unusual and odd thoughts appear in the course of conversation. Even in a schizophrenic remission this irrelevance and vagueness of thought is evident after some minutes. Such type of thinking may be advantageous to the artist and writer or even to the scientist in making original and unusual abstract concepts. In contrast to the weakness of inhibition of thought association, the paranoid patient appears to have the inhibition strongly developed. Once a series of ideas are connected they would seem to inhibit the introduction of any further associations. Each type of thinking may occur in the population at large. The author states that the first type occurs in about 10% of people and indicates the presence of a predisposition to schizophrenia. The second type of thinking is a predisposition to the development of paranoid states.

Special Article.

CULTURE, SOCIETY AND THE MIGRANT.

WELL over a million people have migrated to Australia since the end of the second World War. Assimilation of these people is essential to the future development of the country, and will be greatly assisted if all who are concerned — settled residents, migrants, and those professionally involved at points of contact between the two groups—understand some of the problems that may arise between the decision to migrate and the final successful absorption of the migrant into the population.

Members of the medical profession may be directly or indirectly involved in some of these problems, here discussed in the hope that understanding of them may thereby be enhanced. Why do people migrate? What kinds of people migrate? What physical, social and cultural changes confront the migrant? How may migration affect family life? How may it affect children? Is there a relationship between psychiatric disturbance and migration? What is the impact of the migration programme on Australian society? Is prejudice against migrants a problem?

Migration can be defined as movement of people from a settled homeland to another country, undertaken with the intention of permanently leaving the original homeland and settling permanently in the new country. Assimilation has been defined as a psychological, socio-economic and cultural process, resulting in the progressive attenuation of differences between the behaviour of immigrants and nationals within the social life of a given country (Borrie, 1954). Those who migrate fall into certain classes in terms of ethnic or national origin, socio-economic status, cultural background and religious faith; and an important distinction exists between voluntary and enforced migrations. Patterns of behaviour and of health and sickness are likely to vary from one group to another.

An historical perspective makes the present movement of people about the earth easier to comprehend. Toynbee (1951) has traced the influence over the last ten thousand years of the waves of people who periodically have spilled over from the great breeding grounds of Europe and Asia. We are probably living now in a late phase of a five-hundred-year-old movement of biologically exuberant European man, obliged by rising population pressure or other factors to seek a living outside his homeland. Population growth in the main Oriental foci has had a similar effect—a slow, relentless diffusion of humanity which has been going on for at least as long as the movement of people out of Europe; but while recent demographic changes may slow down the movement of Europeans, Asiatic migrations may continue until the population structure and racial balance of the world are greatly changed. The literature—legendary and scientific—of these wanderings of mankind is enormous. Even that which relates to Australian immigration is considerable (Borrie, 1949, 1954; Borrie and Packer, 1953; Eggleston *et alii*, 1933; Phillips and Wood, 1928). Convicts, free settlers, gold miners, refugees from religious and political persecution, and increasing numbers of people seeking better economic opportunities have all come to this country.

The Nature of the Migrant.

Most historians and sociologists agree that radical removal from a settled homeland to a new and distant country is rarely undertaken in the absence of strong pressure: people are either pushed or pulled from one country to another, in recent years most commonly by economic or political pressure, which may reflect a more fundamental biological pressure of population on living space and natural resources. Perhaps human migrations are ultimately governed by ecological factors in the same way as the distribution and abundance of any other form of life. If so, artificial barriers to the spread of mankind about the earth, whether national boundaries or policies, are unlikely to remain permanently effective: sooner or later rising pressure of population will displace them.

Small numbers of social deviants may leave a country to escape from its restrictions upon them. In this way, any stream of people passing from one country to another will contain rebels from society, malcontents, criminals on the run. Social deviants have at times been most desirable immigrants, as were the Puritan settlers of New England three hundred years ago.

In general it is the young and the fit and the socially unencumbered who migrate. In the case of assisted passage immigrants to Australia, physical fitness is further ensured by medical selection. Huntington (1945) has suggested a rule: the more difficult and dangerous the migration, the better the physical, mental and social quality of those who attempt and survive it. This is a logical extension of the biological law of survival of the fit. The displaced persons who were in the van of post-war immigration to Australia were admitted, for humanitarian reasons, after less strict medical screening than is now practised (Roche, 1960). Nevertheless their record in sport and scholarship, and their attainment of positions of eminence in many walks of life despite the handicaps of language difficulties and a late start, suggest that many are of outstanding physical and intellectual quality. These people are the survivors of a savage selective process which lasted in some cases for more than a decade. Further selection by medical examination hardly seems to have been necessary.

Study of internally migrating groups within the United States of America has shown that complex social and economic factors will determine the social class position and intellectual quality of those who migrate (Klineberg, 1958). Australia at present is receiving immigrants both from economically depressed and overcrowded countries around the Mediterranean Basin, and from Western European countries where the economy is booming, living standards are rising and the population is relatively stable. From time to time there are additional influxes of political refugees, whose migration is enforced. It is reasonable to assume that most voluntary migrants from depressed and overcrowded countries are attracted by Australia's open spaces and rapidly developing economy; but what about the others? What impels people to leave a familiar homeland in prosperous times, to settle in a relatively unknown country? Several motives are possible. They may object to increasing governmental supervision of their lives, as occurs in some crowded European countries, and seek greater freedom by moving to a frontier of western civilization; though if they do, many lack the courage of their convictions, since they remain in cities in Australia, rather than striking out for the "frontier". They may fear calamity in a future war, wish to escape from a potential battleground. They may be adventurers, restless for change and excitement, challenged by the unknown. They may be people for whom "the grass is greener on the other side of the fence". They may have been unable to find a satisfying place in the society of their homeland, either because of their own inadequacy, or because no opportunity exists there for full employment of their particular talent. They may seek a "promised land" where all their troubles will vanish as if by magic, in which case their adjustment to their new environment will be impaired when this expectation is unfulfilled (Hoff, 1958). It is axiomatic that people content with their lot in life do not migrate. When the invitation to migrate is seductively worded and the journey costs nothing, what kinds of people will be attracted?

It is possible only to speculate about the motives which are likely to be uppermost in people's minds when they decide to migrate; and the influence these motives must have on the processes of adjustment and assimilation adds force to the suggestion that investigation is desirable. Psychological assessment as part of the screening process at migrant selection centres is technically possible, and could be expected to assist greatly in our understanding of the motivations, attitudes and aspirations of migrants. If this knowledge could be related to success or failure, to ease or difficulty of assimilation in the new country,

both the nation and its migrants would ultimately benefit. However, it is likely that strong emotional and political objections would be raised were such a scheme seriously proposed.

Some degree of genetic selection may be a consequence of migration; in-breeding within a group of people of common origin and common final resting place may tend to perpetuate some hereditary characteristics (Holmes, 1936). In Australia this may occur among Southern European people such as the Greeks, whose custom is that those first established sponsor the migration of other members of an extended family. This may be of significance in the hereditary transmission of such disorders as thalassæmia, now being seen with increasing frequency in Australia (Wilson, 1960).

Environmental Change.

The impact of the new environment upon the migrant may be physical, social or cultural, or a combination of these. The processes of adaptation, adjustment and assimilation may expose the migrant to the risk of physical or mental disturbance; and the influx of migrants may also expose the residents of the country to certain risks, some of which will be considered subsequently.

Physical Change.

The transition from an overcast Northern European city to the clear sunlight of the Australian countryside may have far-reaching consequences for the skin and the respiratory system. This fact is sufficiently well known to induce some people to migrate in search of better health, though this may no longer be so simple an undertaking as it was in the last century (Thomas and Gandevia, 1959). The desire for better health was a motive for migration for 5% to 15% of internally migrating groups in the United States of America in the depression of the 1930's (Blankenship and Safier, 1940). The proportion is probably a good deal lower in Australia at the present time, although 10 people out of about 500 post-war migrants seen in an Adelaide suburban general practice in 1958 volunteered the information that the quest for a more healthy environment was one reason for their migration. Some people may say that they have enjoyed better health here than in Europe, but such statements are hard to evaluate.

Parasitic microbes not encountered in his homeland may assail the migrant, who will lack the resistance that would have followed exposure early in life; so tuberculosis may afflict people from an isolated rural community, first exposed to the tubercle bacillus when they come to live in an overcrowded city slum (Hess and Macdonald, 1954). Resistance may be further lowered by chronic fatigue due to unfamiliar factory work and long journeys to and fro, and by such common practices as attempting to hold two full-time jobs. Progressive primary tuberculosis does occur in this way in Australia, but it is probably uncommon, as the majority of the migrants, even those from rural areas, have had a primary infection in childhood (Roche, 1960). Nevertheless it may be desirable to detect those at special risk, perhaps by tuberculin skin-testing during their period of ship-board "captivity"; and having regard to their likely social circumstances in this country, it would be logical to protect the susceptible individuals with B.C.G. vaccine.

Socio-Economic Change.

Migration usually involves a change in social status, more commonly downwards than upwards. People of middle class origin will often lose "caste", being subjected to the chauvinism or provincial snobbery by means of which so many Australians succeed in reducing the newcomer, whatever his proper status, to a position of inferiority as a second-class citizen. This may have psychological consequences, for example, leading to a paranoid reaction by the migrant (Listwan, 1956). Refugees, especially those who belonged to the professional classes in their homeland, may be obliged to submit to a profound lowering of occupational and economic and hence social, status, some of which is unavoidable. This may contribute to their maladjustment (Last, 1960).

At the same time there are many migrants who have come from peasant societies with a subsistance economy little above starvation level. Though their status may remain low in Australia, they are economically very much better off than in their homeland. Some begin to move upward through the social classes, excelling in the acquisition of new skills and wealth, which gives them added incentive to accept new social values and cultural patterns. There may be considerable upward class movement in the second generation of these families, and child-parent conflict may then arise, bringing psychological disturbances in its train, in the way that has been observed among immigrant Jewish families in the United States of America (Ackerman, 1958).

Cultural Change.

The importance of the cultural background which distinguishes one society from all others was recognized by William Graham Sumner (1906); but its relevance to medical practice is only now beginning to be realized by a few *avant-garde* health workers and psychiatrists. All migrants, whatever their origin, have to face the cultural differences between their homeland and Australia. The adaptation of peasants to these differences may be particularly difficult, because of the very nature of their existing cultural background, linguistic isolation, superstition, near-illiteracy and limited intellectual horizons. They will find it hard to accept new social values and customs, *mores* and social institutions. Even between closely related societies such as Britain and Australia, subtle differences in attitudes to personal hygiene and accent of speech may lead to misunderstanding. The English and people from some continental countries are reputedly more law-abiding than the average Australian, though this is not likely to increase the Australians' respect for them. Very wide cultural gulfs may separate some alien immigrants from the Australian citizen. What is accepted in one society may be frowned on in another; many people in Australia distrust the street-corner "loitering" which is a folkway of the Latin races, and certainly should not be regarded as delinquent behaviour. The Latin peoples could in turn regard Australian drinking customs with a mixture of amusement and disgust, or just with disgust.

A most important social institution is that of road traffic rules and regulations. Variations between homeland and Australia, together with differences in detail of traffic-conditioned reflexes, may have serious consequences. This is undoubtedly one cause of traffic accidents among migrants from an alien culture.

Language differences are likely to be profoundly important. Sapir (1933) put it as follows:

> Language is a great force in socialization, probably the greatest that exists. By this is meant not merely the obvious fact that significant social intercourse is hardly possible without language but that the mere fact of a common speech serves as a peculiarly potent symbol of social solidarity. . . . The psychological significance of this goes far beyond the association of particular languages with nationalities or smaller local groups. In between the recognized dialect or language as a whole and the speech of a given individual lies a kind of linguistic unit which is not often discussed by the linguist but which is of the greatest importance to social psychology. This is the subform of a language which is current among people who are held together by ties of common interest. . . . "He talks like us" is equivalent to saying "He is one of us."

The existence of this linguistic unit helps to explain the social isolation of some people who speak the language of their adopted country. Inability to detect the subtle shades of meaning of words and phrases, and ineptitude or tactless presumption of familiarity with local argot may lead to something worse than social isolation; a European or an Englishman who addresses his Australian workmates as "Sport" or "Digger" before he has been accepted as one of their number may so affront them as to be ostracized.

Social isolation of the migrant, whether aggravated by linguistic isolation or not, may expose him to special risks. Scurvy has been observed in babies whose immigrant parents have had no one with whom to compare notes on child rearing (Clements, 1960); and a case has been recorded of a family who threw away the mushrooms gathered on a week-end walk, but ate the toadstools (Last, 1960).

The housewife who is isolated from her neighbours by language barriers, and perhaps has only infrequent contacts with members of her own cultural group (even sometimes her own family), is likely to be particularly vulnerable to the adverse consequences of her isolation. Her inability to communicate may cause her much misery, especially when she is uprooted from her familiar little world, as she is by illness or childbirth. It is common for doctors and nurses in hospitals to speak disparagingly of the "low pain threshold" of such people; yet they bear great suffering with fortitude. Perhaps it is the aseptic unfamiliarity of a hospital that is too much for them. The screams of such a woman may be the expression of terror she would not feel among members of her own group in familiar surroundings. It is particularly unkind to deprive her of the solace of visits from a large tribe of her relations, even if the hospital ward is temporarily rendered a little untidy; nor should it be forgotten that the hospital may have for her an emotional association of disease and death uncommon these days in a medically sophisticated culture.

Family Patterns and Migration.

The processes of migration and assimilation may disturb the normal pattern of marriage and family life in several ways, some of which have demographic implications.

Husband and wife may be separated, sometimes for years, by the exigencies of establishment in the new country. The wife will then arrive to be confronted by a prepared home and a husband who has made his adjustment to the new life; but he may have become almost a stranger to her, and her adjustment to him and to her new life in Australia may be impaired by her cultural background and her linguistic incompetence. Moreover, the years of separation have been lost out of her reproductive life, which may matter in a country which is trying to build up its population as rapidly as possible. The girl who is a proxy bride, married by arrangement to a man she has never met, probably a man ten or more years her senior, often seems to settle down surprisingly well, in this case no doubt assisted by her cultural background and upbringing in a society where women are subservient to men. Nevertheless, a statistical study may confirm the widely-held clinical impression that these girls have difficult, stress-affected pregnancies, probably for reasons connected with their linguistic and social isolation.

Some people place a higher value on economic and social establishment than on procreation. Migrants of middle-class origin, reduced to straitened circumstances in the aftermath of war, may come to Australia with a heightened appreciation of the material comforts of life, and it is then common for the wife to forsake her rôle as mother and home-maker, so that her wages augment the family income, assisting the restoration of socio-economic status. This may make necessary the prolonged use of contraceptives, a practice which is said to produce organic gynæcological disorders, and which may also have psychological consequences. When there are children in the family, they are likely to be inadequately cared for while both parents are away at work. Sometimes the parents may attempt to divide between them the responsibilities of child-rearing by working different shifts, and may succeed until interrupted by circumstances like illness. Undesirable customs of this kind are by no means confined to migrants; but the incentive to behave in this way seems strongest in just these very people whose social isolation exposes their children to the greatest risk of neglect. This is one situation encountered in medical practice where tactful intervention in the internal affairs of the family is justifiable. Sometimes one spouse may accept and the other reject the facts of life in the new country, so setting the stage for an explosive marital battle.

Australia has always attracted more male than female migrants, from convict days through the gold rushes to the present time, when forlorn notices in the "Personal" column of the classified advertisements in the Press, and scribbled slogans on walls, attest to the woman shortage among migrant men. Single male migrants, denied a wife by mathematical odds as well as by social isolation, constitute another section of the population whose fertility is impaired by migration. They may also have serious social and psychological problems, living in squalid lodgings, condemned to celibacy and emotional deprivation which will sour their enjoyment of work and of living. Their problems may be aggravated if they gain too much insight into their situation, unaccompanied by the hope of better things to come. A lonely refugee migrant committed suicide after a medical interview in which he was tactlessly questioned and attempts at psychotherapy had failed.

Large numbers of single men, usually of Southern European origin, sometimes live under extremely congested conditions in slum areas, sometimes six or eight sleeping in a room meant for two or three. Bathroom and laundry facilities, kitchens and meals are often primitive and makeshift, and the most elementary principles of hygiene may not be observed. Gastro-enteric infections are likely to be endemic under these circumstances, respiratory infections including tuberculosis could have a high morbidity, and venereal disease is common among men in this social class. The psychological consequences of this kind of congested and uncongenial living conditions are often hard to assess because of language barriers; but a morbid preoccupation with minor ailments out of keeping with mental good health, and "malingering", which implies some psychological upset, are common.

The Effect of Migration upon Children.

Children start life in a new country from nearer scratch than their parents, because of the ease with which they can adapt themselves to new customs and new loyalties, and can learn, when necessary, a difficult new language. However, they may suffer several handicaps, such as those already mentioned in relation to social isolation.

At the time of embarkation for Australia, children can be given gamma globulin, which, if all receive it, may prevent a major ship-board epidemic—for example, of measles. The protection conferred by this injection has worn off by the time the children arrive in Australia, so outbreaks of infectious disease may occur if many are obliged to stay for long in migrant hostels. However, an epidemic under these circumstances can be managed without great difficulty.

The consequences of psychological maladjustment are probably most devastating for children. Not only will the physical home have been disrupted, the familiar world disintegrated by the migration, but quite often the whole atmosphere of family unity, affection and security may be upset. There is a period in hostels and on the ship when parents may be too preoccupied by the struggle for a place in the queue for this or that necessity to give the children the affection and reassurance that they need. This will be particularly likely to happen when a parent, especially the mother, is already a psychological casualty. Under these circumstances the children may resort to their peer-group, a leaderless rabble of bewildered little outcasts. The phenomenon of "camp psychosis" (*Lancet*, 1960), a state of apathy or emotional depression which develops in people confined for years in refugee camps, their hope of salvation slowly dying, will aggravate the tendency towards disturbance in their children.

After arrival in their new country, children may, in the absence of adequate parent-figures, identify with the loudest, most aggressive, most dramatic group in the environment, perhaps the local gang of juvenile delinquents. The great vulnerability of the solitary child, and the deleterious effect of disrupting the parent-child bond, are important in this context.

Parent-child conflict may be subtle and insidious. In any case, children will develop loyalties to the members of their peer-group at school, relating them to their new country. Their parents, on the other hand, are more likely to cherish and preserve the traditional customs and beliefs of their birthplace, destined perhaps to survive as a "Paradise Lost" of folklore. Conflicting loyalties may then appear in the family, and although this probably gives rise but seldom to clinical problems, it may do so—for example, among people whose national group is strongly cohesive and abides by a rigid code of behaviour.

> A young Greek-born woman, educated and working for her own living in Australia, was obliged very much against her will to follow her people's custom of contracting a marriage, arranged by the two sets of parents, with a man she hardly knew, 12 years her senior. She became acutely neurotic. She said she objected not so much to the arranged marriage as to the fact that she had not been permitted, like her Australian girl-friends, to learn a little about men by mild flirtations and boy-girl friendships from her school days onward. Her insight and her intelligence enabled her to express clearly how much she resented being a captive slave of alien tradition in a land whose freeborn ways she had discovered.

How frequent and how deep-seated is child-parent conflict in migrant families? What part does it play in the pathogenesis of delinquent behaviour? How frequent is delinquent behaviour in migrant children? When delinquent behaviour does occur, how often is it vicious, how often an expression of a sense of release from the social inhibitions of the homeland, how often apparent rather than real, indicating different social *mores*? What influence have imported patterns of child-rearing and parental attitudes on the behaviour of migrant children? At best we have patchy and incomplete answers to one or two of these questions (Klineberg, 1958; Wootton, 1959), and no answers at all to the rest. The recent report on the assimilation of migrant children (Dovey *et alii*, 1960) stimulates thought more by the questions it leaves unasked and unanswered than by what it has attempted to ask and to answer.

Psychiatric Considerations.

Many workers have noticed the high incidence of schizophrenia among migrants, usually ascribed to the schizoid person's restless search for solitude, which leads him to forsake family and friends, to run away from familiar places (Hare, 1952; Mezey, 1960). It would be beyond the scope of the most searching medical examination to detect many of these people before they migrate, and even the very seriously disturbed may evade detection if the medical examination is hastily conducted by someone who does not speak the same language.

Adjustment to the new country may involve far more psychological trauma than the migrant had anticipated when he left his homeland. He may have been misled or inadequately informed about the way of life he will encounter, or may have imagined that migration will involve no more than would a move to a new house in his home town. The impact of the change will fall unequally upon different members of the family, depending on such factors as age, sex, occupation, degree of exposure to stress, and probably most important of all, preexisting state of mental health. The preeminent importance of mental stability as a factor in successful adjustment of voluntary migrants has been demonstrated in a carefully controlled study carried out in Israel (Weinberg, 1955). Some psychiatric disturbance may be directly due to the environmental change alone, though it is obvious that the stresses of migration are more likely to unbalance those who are already unstable. Emigrants from Norway break down more often than Norwegians who stay at home, for one or other of these reasons (Ødegaard, 1932).

Cultural and social factors lead to varying concepts of what is normal behaviour; and rapport is difficult across cultural and social barriers, even in the presence of a common language, adding to the difficulty of psychiatric assessment (Carstairs, 1958). An important preventable psychiatric disturbance is the individual or group paranoid reaction which tends to develop in people isolated from the rest of the community by language barriers and cultural differences (Listwan, 1956, 1959). Social agencies such as the Good Neighbour Council may greatly assist in breaking down the barriers from both sides. The foreign language Press, with its functions of presenting news of the homeland juxtaposed with news of migrants' doings in Australia, and its implied or actual editorial policy of assisting assimilation, has a most important rôle (Zubrzycki, 1958). At the individual level, those having professional contact with migrants can assist assimilation by helping them to use their own resources effectively, and by describing their situation accurately and sympathetically to other people and organizations in a position to help them.

The Impact of the Migration Programme.

It is hardly necessary to say that migration since the last war has added immeasurably to the material wealth of Australia. The cultural development of the country, to which the contribution of migrants has been enormous, is just as spectacular. Whatever one's interests—music, painting, architecture, delectable ways of preparing food, or just watching football—one must acknowledge the recent injection of talent from overseas, and be thankful. Slowly and subtly the insularity and parochialism of Australians seem to be breaking down in the presence of increasing numbers of people who can perceive and appreciate variety in customs, interests and style of living.

A small price may have to be paid for these blessings. Some migrants may bring with them diseases previously not present in the country, such as leprosy, which was brought into northern Australia by indentured Asian labourers. Such conditions as tapeworm infestation may become established in areas where intermediate hosts are present and standards of hygiene and sanitation are poor. The fertilization of market gardens with human excreta is a common custom among some classes of immigrants, though it seems to lead to outbreaks of disease surprisingly infrequently. Some years ago a fire in a public lavatory in the Central Market of Adelaide drew the attention of health authorities to an odd problem to which so far no satisfactory solution has been found. It is the custom of people from some parts of south-eastern Europe to burn the paper with which they clean themselves after defæcation. Attempts to educate these people to the proper use of water-closets have failed; inspectors still find little heaps of ashes or of partly combusted paper contaminated with excreta on the floors of public lavatories in this part of the city.

In general it is probably true that the risk of introduction of serious organic disease by immigrants to Australia is slight, and that such diseases as may be introduced from time to time can be controlled without great difficulty. The emotional impact of any immigration programme may be more far-reaching, and have more permanent consequences. These deserve special mention, even though their medical importance may be slight.

The Problem of Prejudice.

Williams in 1947 wrote as follows:

> Migration of a visibly different group into a given area increases the likelihood of conflict; the probability of conflict is the greater (*a*) the larger the ratio of the incoming minority to the resident population; and (*b*) the more rapid the influx.

Prejudice against minority groups may become a very serious obstacle to successful assimilation. To date there are few important minority groups in Australia; but the understandable tendency for people of common origin to live reasonably close to each other, and the aggregation of national groups at regional centres where they follow a common occupation or industry, must encourage this development.

We may have to ask ourselves, as Allport (1954) does in his monograph, whether the amalgamation of all groups is a valid ideal, or whether we should strive to maintain as much diversity and cultural pluralism as possible—in

other words, should our aim be the assimilation or the integration of migrants from another culture? Allport defines social and psychological factors which encourage prejudice. Among the social factors are social heterogeneity, vertical class mobility and rapid social change; barriers to communication and large minority groups; and sanctions against assimilation. All but the last of these, and traces of this in places, can be discerned in Australia.

The study of the psychodynamics of prejudice has become a matter of some urgency in several parts of the world. Prejudice is a very satisfactory outlet for the basic aggressive drive common to all humanity, and will often flare up against a minority group when a scapegoat is sought to blame for some serious social reverse; prejudice against migrants has been observed at several times of economic crisis in Australian history (Bailey, 1933). People with immature personalities are most likely to exhibit prejudice, which may become closely linked to ideas about sex and the sex instinct, the target group being considered to have animal-like sex appetites. This may become important when there are discriminatory or prohibitive sanctions against intermarriage. Some sanctions do exist in Australia: people of northern European origin are often opposed to the idea of intermarriage with the recognizably different people from southern Europe. Thus there already exists an adverse attitude to what some authorities regard as a genetically desirable state of affairs (Medawar, 1959; Burnet, 1959). The effects of prejudice may become grievous in marriages between migrants and Australians, when both parties have to bear the brunt of this adverse attitude, emanating from their respective family and friendship groups, in addition to their own difficulties of adaptation to each other.

Propinquity tends to destroy prejudice, at least partly, because it helps to modify social attitudes, even when the prejudice is based on major racial differences (Deutsch and Collins, 1951). Attempts to determine the degree of mixing and segregation of migrants which is taking place in Australia have been only partly successful (Rose, 1958). On a small scale in a suburban area of Adelaide, both sides of the picture are clearly to be seen; in one street of 80 homes, people from at least 15 nations live amicably side by side, traditional enmities forgotten, especially by the children, who play together in the street at their own versions of cricket and Australian Rules football. Near by is an area of some half-dozen streets occupied almost exclusively by people of Greek origin, many of them living under conditions of extreme overcrowding, each bedroom in the house being inhabited by an entire family, often with several children. Their standards of hygiene are low, and their strange ways and foreign speech have greatly disconcerted some of the Australian people in the neighbourhood. But even when the standard of living of the migrants is comparable with local standards, prejudice can show itself through the agency of the stereotype, a kind of mental economy by which the members of a group are all perceived as possessing the same common characteristics, despite their very real individual differences. When prejudice exists, the stereotype is constructed of all the undesirable qualities, and is expressed in such a form as "all migrants have low moral standards, are out for what they can get, and supply most of the country's criminals".

In a world whose rising population has revived memories of the gloomy prophecies of Malthus (1798), we must expect Australia to receive increasing numbers of migrants from areas where population pressure has depressed the living standards to levels far below those to which we are accustomed, and we must expect to receive many more people of recognizably different ethnic origin from the majority of the present inhabitants of the country. The problem of prejudice is only one of many that may then arise, though it may certainly be amongst the most difficult. We should be preparing now to meet these problems.

Summary and Conclusions.

In this paper I have considered some of the problems related to the assimilation of migrants, rather than migration *per se*. Consequently the hazards and the medical problems that may arise before and during the actual migration have not been discussed, for they do not as a rule bear on assimilation.

To define a problem is not to solve it. Consideration of solutions to some of the problems here discussed is beyond the scope of this paper, but it is hoped that definition of those which may involve the medical profession will assist understanding and so make a little easier the process of assimilation. Our ignorance is revealed when some of the problems are stated, and several worthwhile avenues for research are apparent.

Even in the absence of medical screening, migration is a selective process. Those who migrate are self-selected by their ability to move, which will vary with such factors as age and physical fitness and social position; and they are selected also by qualities of personality such as motivation, attitudes and aspirations. The personality of the migrant will modify his ability to become assimilated, but precise information on the nature and degree of this modification is lacking. In a country which depends on the success of its migration programme as much as Australia does, critical study in this field is most desirable.

Psychological adjustment is implicit in the definition of assimilation, and the possibilities for maladjustment are numerous. In addition to the changed physical environment, adjustment to which may require some acclimatization, the migrant faces changes in his socio-economic status and cultural environment. The likelihood of maladjustment always exists, and will be aggravated both by adverse environmental circumstances and by defects in the migrant's personality. The migrant may be linguistically and socially isolated, which will add to his difficulties.

Migration may modify the normal pattern of family life in several ways. Husband and wife may be separated, or they may have to change traditional family rôles to ensure economic establishment; and numerical inequality of the sexes or social isolation will preclude marriage for some. Several social and psychological problems related to the marital patterns and behaviour of migrants can be defined.

The children of migrating parents may be particularly vulnerable, if their parents cannot cope with the problems of the move, or are too preoccupied getting established in the new country to care adequately for them. The interaction between parents and children in relation to the social and cultural changes of migration is a subject which deserves critical study.

Several forms of mental illness can be related to migration: schizoid individuals may find solitude by migrating; and social, cultural and linguistic isolation of the migrant may induce a paranoid reaction. Mental stability aids assimilation, and ease of assimilation fosters mental health.

Migrants bring great benefit to the nation, but we must watch for troubles that may attend their coming. The somatic afflictions accompanying migrants may be slight, but the psychosomatic illnesses and emotional turmoils both of migrants and of residents may be considerable. An appreciation of the migrant's social, cultural, vocational and domestic situations, and awareness of the prejudice he may have to negotiate, should lead to better understanding and wiser counsel from medical practitioners. So the process of assimilation may be facilitated, and this is surely good preventive medicine.

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J. M. LAST,

North Adelaide, South Australia.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 29, 1960, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. B. A. COOK, the President, in the chair.

Hæmolytic Disease of the New-Born.

DR. S. E. J. ROBERTSON read a paper entitled "Hæmolytic Disease of the New-Born" (see page 398).

DR. W. G. MCBRIDE read a paper entitled "Hæmolytic Disease of the New-Born" (see page 403).

DR. M. D. MANION read a paper entitled "Erythroblastosis Fœtalis—Random Thoughts" (see page 405).

DR. R. H. VINES, in opening the discussion, said that he had been interested in Dr. Robertson's modification of the long-used criteria of Mollison and Cutbush, including a hæmoglobin value of 13 grammes per 100 ml. There was a lot in his favour there. Experience at the Women's Hospital, Crown Street, suggested that such a figure might well be better than the higher figure used before. Dr. Vines said that a serum bilirubin content of 4 mg. per 100 ml. rather frightened him; bilirubin should not be allowed to reach that level before exchange transfusion was decided upon. Dr. Robertson had said that he was upset by the use of clamps on umbilical cords; how long did he leave the cord before the first exchange transfusion? Dr. Vines went on to say that the signs of kernicterus might be very transient, and the pædiatrician on his daily visit might easily miss them. The responsibility of observing them might rest in the hands of an experienced nursery sister. Referring to Dr. McBride's paper, Dr. Vines said that one or two points in it appealed to him very much. The first was his plea that babies known to be affected should be born in the hospital where they were to be treated. The rule was disregarded far too much in Australia. Dr. McBride had also said that only one in 3000 babies with A B O incompatibilities needed exchange transfusion; Dr. Vines was sure that they had exceeded that figure at Crown Street in recent years. The fact that at Crown Street there was still a 23% loss in that disorder showed how far they still had to go. The question of induction of labour was very important; over the years mentioned, there had been a restriction of that practice at Crown Street. Dr. McBride and Dr. Manion had suggested that help should be sought from the newer techniques, such as amniocentesis, which were used in Melbourne. Dr. Vines said that he could not help feeling that the mother's antibody titre still deserved some attention. It was getting attention in Melbourne, and had long received it in Western Australia. Dr. Vines said in conclusion that he only wished he could answer some of Dr. Manion's questions.

PROFFESSOR T. STAPLETON said that he was glad to hear that the principle was accepted that whenever there was a possibility that an affected baby would be born, the mother should be delivered in a hospital equipped to provide a twenty-four-hour pathological service to deal with the situation. If there were parts of New South Wales in which that was not so, it should not be too difficult to remedy. Such action might result in a greater reduction in mortality due to kernicterus than mere attention to the technicalities and refinements of treatment, if they were confined to patients in the teaching hospitals.

DR. R. S. HYSLOP said that he had been glad to hear Dr. Robertson say that the treatment of severely affected babies should be begun as soon as they were born. At King George V Hospital they used amniocentesis to predict how the baby would be at birth. When they knew that an affected baby was to be delivered, they were ready with blood to give an exchange transfusion and any necessary pathological investigations were made simultaneously. All that it was necessary to know at once was the hæmoglobin value—the serum bilirubin content was of secondary importance. Dr. Hyslop said that he agreed in theory that at the age of three or four days the baby should have a direct serum bilirubin content of 5 or 6 mg. per 100 ml. However, he had yet to find a figure of greater than 1·6 for direct-acting bilirubin, even in babies aged seven days. Commenting on a statement by Dr. McBride, Dr. Hyslop said that he could not agree that it was unfortunate that one-third of severely affected babies died before 36 weeks of gestation. Surely that was something to be thankful for.

Prenatal investigation by amniocentesis would show which patients needed to have labour induced at 36 weeks or later. It was the other one-third that had to be fought for. Their chances were very slim; but at King George V Hospital they had delivered babies alive before 36 weeks. He did not think that amniocentesis really worried the mothers after the first time. There was no morbidity attached to the procedure. On the question of the effect of drugs, Dr. Hyslop said that people were now beginning to realize that "Gantrisin", vitamin K and probably other drugs competed with bilirubin for albumin and therefore kept the level of bilirubin up. That might result from the transfer of drugs from mother to fœtus. Dr. Hyslop said that he had been glad to hear Dr. Manion say that when a decision to induce labour had been made, it should be done at once and energetically. Amniocentesis would provide the answer to the question whether it should be done or not; it told what the state of the fœtus was. He was sure that until some better way was found, it provided the only means of getting that information. One of its greatest uses was in the case in which the husband was heterozygous.

DR. W. CARY said that he wished to reinforce some of the remarks made by Dr. Hyslop. He agreed that things were not quite so dark as Dr. Manion had painted them. By amniotomy, he could tell him just how bad the baby was and when to induce labour. They had delivered quite a number of babies at 32 weeks. Certainly they were premature, but they were alive. One or two were now aged 18 months, and were well. Dr. Cary agreed with Dr. Manion that obstetricians would sometimes fiddle. Labour had to be induced quickly. If the patient did not go into labour, Cæsarean section had to be performed. The pædriatricians could do better if the babies were delivered vaginally, but it was impossible to wait if they were severely affected.

DR. T. L. ROBERTS said that he came from Lismore, and that he rose in defence of the country. Their chief problem was A B O incompatibility, and the trouble arose when the child was aged 16, 18, 24 hours. The only solution was to offer more services to the country. They could handle at the base hospitals A B O incompatibilities that they knew were going to occur; they could not handle those that took them by surprise.

DR. GRACE CUTHBERT BROWNE, referring to the management of Rh-negative mothers away from teaching hospitals, pointed out that in a survey of deaths from hæmolytic disease occurring in 1958 the following factors had been revealed.

Routine tests during pregnancy had not been done. Such tests fell into two groups. The first consisted of routine Rh testing, routine blood grouping, routine blood tests and routine hæmoglobin estimation. The second omission was routine estimation of agglutinins. That meant failure to exclude (i) previous blood transfusion, (ii) previous intramuscular injection of blood or (iii) previous pregnancy or miscarriage not known to the medical practitioner in charge of the current pregnancy.

Referring to exchange transfusion of the infant, Dr. Cuthbert Browne said that there was (i) failure to give exchange transfusion early enough, (ii) failure to recognize when a second exchange transfusion was indicated, (iii) failure in technique during transfusion, (iv) failure (when the result of the Coombs test was negative) to estimate the serum bilirubin level, to ensure that an exchange transfusion was or was not indicated.

Dr. Cuthbert Browne then referred to the necessity for meticulous observation of new-born babies during the first 48 hours, to watch for the occurrence of jaundice, and stressed the importance of failure to recognize the severity of jaundice and its significance. She said in conclusion that sterilization at Cæsarean section for Rh incompatibility in young women was contraindicated for obvious reasons—for example, change in marital status, etc.

Dr. Robertson, in reply, said that he entirely agreed with Dr. Roberts. Many affected infants were handled at the Royal Alexandra Hospital for Children, and he asssured country doctors that if such infants were sent to that hospital early enough, they had every chance of a full recovery. There was no need to send the mother down to the city for her confinement unless she had a history of a previous severely affected infant. In any case, many country mothers would not agree to coming to the city to have their baby in strange alien surroundings, amongst strangers, even if they could afford it and could make arrangements for their other children to be looked after. Dr. Robertson stressed the need for improved pathological and pædiatric facilities for the diagnosis and management of the disease in country centres. To embark on a policy of sending mothers to the city for delivery could mean that over 6000 women could descend on Sydney each year. In reply to Dr. Vines, Dr. Robertson said that before inserting a catheter to carry out an exchange, he left a piece of cord about as long as the distal phalanx of his thumb—about one inch. The figure of 4 mg. per 100 ml. of bilirubin in cord blood as an indication for immediate exchange transfusion had been worked out from his own experience. Very rarely did an infant with a figure less than that eventually require replacement transfusion. Finally, Dr. Robertson said that Dr. Hyslop should check with his biochemist as to the technique used in estimation of direct-reacting and indirect-reacting bilirubin levels in serum. It was most unusual not to find a rising proportion of the direct variety from the third day onwards, when the level of total bilirubin was remaining stable or increasing.

Dr. McBride, in reply, said that Dr. Vines had misunderstood him; he had said that A B O incompatibility occurred in one of every 300 deliveries. He did not rely on antibody titre alone as an indication that the baby would give a positive reaction to the Coombs test. It seemed that Dr. Hyslop was not worried about hyaline membrane, but Dr. Cary was. Dr. McBride said that he could not quite agree with Dr. Robertson—his remarks had been directed at some city centres. He could name several large hospitals not far outside the city of Sydney where, if an affected baby was born at night, the pædiatrician might see him next morning, the pathologist would do his work later, and as much as nine hours might elapse before the diagnosis was made. Dr. McBride thought that it would be a good thing if some country women were brought to Sydney for their confinement.

Dr. Cook, from the chair, said that those present had enjoyed a stimulating evening. The papers and discussion had shown that the problem was being regarded seriously, and the question of infant mortality was being pushed forward as of urgent priority.

Out of the Past.

THE BUBONIC PLAGUE.

[From the *Australasian Medical Gazette*, March 20, 1902.][1]

LAST week there were [in Sydney] seven cases and two deaths; the previous week there were seventeen cases and five deaths; the week before that saw nine cases and four deaths recorded. Up to the present there have been sixty-three cases and seventeen deaths. At the Coast Hospital on Saturday thirty-two patients remained under treatment . . . From March 1st to March 7th, the total number of rats taken to the depôts established by the Board of Health was 4,419. Including the number destroyed by the men fumigating coastal vessels, and the sewers, quite 7,000 must have been accounted for, in addition to many thousands more killed by residents in Wednesday's rat crusade, of which no record will ever be obtainable.

Correspondence.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: One is in whole-hearted agreement with Dr. E. S. Stuckey (MED. J. AUST., September 17, 1960) in his criticism of the Pharmaceutical Benefits Scheme. The present scheme, evolved by the union of two incompatible components, is based on unsound principles which will never allow it to become really satisfactory. Bearing in mind that the primary aim of a benefits scheme is to ease the cost burden of medicines for the working man, so that health considerations are not jeopardized by high cost, it is worthwhile to consider the requirements to which the ideal scheme should attain.

1. All medicines for which a prescription is usually written should be available; then: (*a*) The patient is not penalized because the best treatment for his particular case is not available on the Government list. (*b*) The patient is in a

[1] From the original in the Mitchell Library, Sydney.

position to take advantage of the most recent developments in therapy. A Government list, by its very nature, can never be up to date. (c) The doctor is not faced with the artificial consideration that an expensive listed drug be prescribed because it will cost the patient only 5s. instead of a cheaper but unlisted form which would cost him more than 5s.

2. Medicines should be available in the quantity required by each individual case. A set list does not satisfy this requirement. Sometimes the quantity is insufficient, in other cases it is excessive and leads to wastage—wastage, because there is no saving to the patient if one prescribes far less than the maximum quantity; he still has to pay the full set rate. At present, repeats of a prescription written for less than the maximum quantity are not allowed. The reason for this was obvious in the old "free medicine" days, but in practice today, often leads to wastage.

3. The ideal scheme would function with a minimum of red tape—that is, it would contain its own intrinsic controls to replace control by external rules and regulations. The present Pharmaceutical Benefits Scheme, a flat-rate scheme, is not attuned to any of these three requirements. The use of a flat-rate scheme necessitates the imposition of a limited "official" list of drugs allowable only in certain quantities and sometimes only for certain conditions. Further, its lack of any integral, built-in controls necessitates a complex of external regulations to prevent abuse.

If we used instead a percentage scheme, where the Government paid, say, 80% of the cost of each prescription, and the patient paid, say, 20%, then such a scheme would contain its own intrinsic controls. It would be self-regulating, in that the cheaper the drug and the smaller the quantity used, the less it would cost the patient. Savings achieved by the doctor in prescribing would thus benefit the patient directly. This is the way things worked successfully twenty years ago, and there seems to be no sound reason for discarding the nice balance of natural controls in favour of the clumsiness of external regulations. The Government appears to have no conception of the tremendous importance a doctor attaches to the best interests of his patient. During a consultation, one is not at all concerned with the national economy, but solely with what is best for the patient. The only efficient and satisfactory way to encourage economical prescribing is through the doctor's efforts to avoid unnecessary expense for his patient, and with a percentage scheme this would automatically be achieved, not only saving the patient money, but even more so the Government, which bears the greater proportion of the cost. All medicines for which a prescription is usually written would be available, and the percentage scheme would automatically do away with the need for restriction of quantity. There would be little or no need for restriction as to usage, since the control can be achieved more positively by expert advice at lectures, refresher courses, articles in THE MEDICAL JOURNAL OF AUSTRALIA and per the B.M.A. bulletin, than by government regulations.

There should not be an official list of subsidized drugs. It is unrealistic to draw up a list of expensive drugs and propose that these will be the only ones subsidized, since this will only lead to their excessive use. Any limited list must inevitably suffer from this defect according to the degree of limitation. That the Government will insist on some form of limitation is, however, certain. The qualification that all medicines should be available "for which a prescription is usually written" would automatically exclude such items as "Akta-Vite" and "Dietrole". Whether the general run of vitamin preparations and tonics should be included would need consideration. But any such restriction would simply be a blanket exclusion of easily defined groups of drugs. Thus, we would not have the present stupidity of a list which includes "Largactil", but not "Sparine" or "Vallergan"; "Sodium Amytal" capsules, three grains, but not one grain; 'Probanthine", but not any of its less expensive congeners; antihistamines for adults, but none for young children who cannot swallow tablets; and which includes "Butazolidin", but allows it only for the elderly, to whom it is most dangerous. Any practising doctor could list hundreds of similar anomalies.

On analysis, the existing flat-rate scheme has so many inherent and fundamental defects that it can never approach the ideal, whereas the suggested percentage scheme, possessing its own inbuilt incentives and controls, can approach very closely to the requirements outlined at the beginning of this letter. The actual percentage payable would depend on how much the nation could afford, and variation of the percentage would provide the Government with a very flexible form of control, which is not readily available with a flat-rate scheme.

Operating a percentage scheme could be quite simple. The doctor prescribes the best and least expensive available medicine in the most suitable quantity, and the patient pays the chemist 20% of the cost. If it costs 10s., the patient pays 2s. If it costs £10, the patient pays £2, and he is saving £8, which is still a fair deal. The chemist copies the prescription into his book as usual, and sends the original, priced and stamped, to the Department of Health for reimbursement. Repeats would be handled by the chemist issuing a repeat authorization, on which he would also enter the full prescription, with the same reimbursement procedure. There is no real need for duplicates. The whole operation can be carried out at a pharmacist-Government level, without any need for direct participation by the doctor. The Pensioner Medical Service could easily be incorporated. The chemist notes the pension number from the pensioner's card on to the original prescription and any repeats. Government reimbursement would then approach 100%.

In spite of the fact that a percentage scheme offers the advantages of making any medicine necessary available to the patient, in whatever quantity is necessary, without great financial hardship, with a concomitant incentive to economy on the part of the doctor, and in spite of the fact that it offers a considerable reduction of red tape with complete abolition of the present stupidities and inconsistencies, with the certainty that the taxpayer will receive much better value for each pound of tax money spent, we cannot expect the Government to accept the scheme simply on its merits. The Government cannot and will not accept any basic alteration to its present scheme, unless it is forced by the pressure of public opinion. Therefore, the public must be informed of the faults of the present scheme; that it is stupid, unfair and wasteful. It is up to ourselves to initiate consultations between the Pharmacy Guild, the British Medical Association, the drug manufacturers and other interested bodies. Proposed improvements must be agreed to and formulated, and a plan for public education decided upon and put into effect. If a small proportion of the colossal advertising expenditure of the manufacturers could be diverted to inform the public of the serious shortcomings of the present scheme, and the improvements which could and should be made, it would not be difficult to organize awakened public opinion to exert a formidable pressure. For instance, towards the end of such a campaign, 10,000 practising doctors could easily collect on a public petition 1,000,000 signatures. The Government can choose to ignore the advice of the medical profession, but it must respect the opinion of 1,000,000 voters.

The Minister for Health has said that the scheme will never satisfy everybody until it includes all medicines, and he is quite right. It will not. It will not be satisfactory until the patient can receive whatever medicine he needs, without hardship. Such a general scheme needs its own inherent incentives to economy, to avoid wasteful or extravagant prescribing, and this can be satisfactorily achieved only by a percentage scheme.

Yours, etc.,

DON MARR.

267 Bobbin Head Road,
North Turramurra,
New South Wales.

Undated.

QUADRUPLE ANTIGEN.

SIR: The letter from the Secretary of the National Health and Medical Research Council in the Journal of February 25, 1961, is reassuring in so far as it refers to the poliomyelitis component of quadruple antigen; but the fact that the advising subcommittee, even though composed of men of the greatest eminence, advised that immunization should be commenced in the sixth (*sic*) month after "having considered recent experience of pertussis in Australia" must stand up to examination.

Firstly, the eventual recommendation as given in the pamphlet issued by the Public Health Department of New South Wales recommends that quadruple antigen injections be given to children from the age of six months onwards—i.e., in the seventh month.

Secondly, statistics obtained from the Bureau of Statistics and Economics of New South Wales give the following information: in the years from 1957 to 1959, whooping-cough was implicated in the deaths of 24 persons in Australia (nine in New South Wales), these figures not including deaths in aborigines containing half or more native blood. Fourteen of these cases occurred in 1959 (five of them in

New South Wales). Broken down by age, the figures show that eight deaths occurred between birth and three months, ten between three and six months, two between six and twelve months, three between one and three years, and one in adult life. These figures are small, but do indicate that very many cases of whooping-cough occurred in the relevant years in the age group from three to six months—this is in accord with past experience and is the reason for the established recommendations over the last ten years that immunization against pertussis should be started as early as possible in infancy; it is entirely possible that "recent experience in Australia" has been favourable only because the majority of children are immunized against pertussis, and with most of them immunization has been commenced at three and not six months.

Thirdly, my own recent experience of pertussis in the small part of Australia with which I am concerned is that I have seen no less than eight cases of pertussis in six families without obvious direct contact in the last four months; this is more than all the cases I have seen in the previous eight years.

I still have the temerity to maintain that to use the quadruple antigen, commencing at six months, is to sacrifice the principle of early protection against that one-time deadly disease of infancy, pertussis, for the expediency of adopting the neat and attractive production of the technologically brilliant staff of our immunological laboratories. The gain will be that babies have two fewer relatively undisturbing injections; the loss will be that every child born will be exposed for an extra three months to the dangers of contracting pertussis with its attendant morbidity and mortality.

The scales, sir, do not balance.

Yours, etc.,

A. K. McKELLAR STEWART.

789 Forest Road,
Peakhurst,
New South Wales.
March 1, 1961.

AN AUSTRALIAN MEDICAL ASSOCIATION.

SIR: Now that the draft of the Federal Constitution of the Australian Medical Association is nearly complete, consideration is being given to alterations made necessary in the constitutions of the State Branches so that they shall conform. In New South Wales it is the intention of the Branch Council to place before its members that an alteration be made in the manner of election of the members of the Branch Council, but I am informed it is intended to leave the Branch Constitution unchanged on other principles.

It would seem highly desirable that we should also review the powers of the Branch Councils to act on behalf of the members of the Association. At present the powers of a majority of the State Branch Council are absolute in matters affecting the Branch and its members.

Many of us are of the opinion that when the State Council is called upon to enter into agreements, either with governments or other organizations, and these agreements are likely to materially affect the social or economic status of the individual members of the Branch or shall alter or vary the working conditions of the individual members of the Branch, then the Branch Council should be obliged to stand fast on the *status quo* until such time as the opinions of the local associations have been expressed to State Council. When these opinions have been made known to Council, they shall form the basis of the new agreement entered into by the Branch. If there shall be any matters which the State Branch Council considers should be included in the new agreement, but which are at variance with the opinions expressed by the majority of the local associations, then these matters must be referred back to the local associations for their further consideration before being made part of the final agreement. Provided, however, that in an emergency the unanimous vote of a meeting of the full State Branch Council may be substituted for the acquiescence of the majority of the local associations.

A similar state of affairs should also apply when Branch Councils are to acquiesce on new government legislation or new government regulations. The State Branches should demand that the effecting regulations be withheld until ample time for consideration has been given to the Association's members.

Such clauses built into the constitution of the State Branches will act as buffers against sudden political pressure, as was applied to the Federal Council over the Pharmaceutical Benefits legislation. At the same time it will prevent the introduction of agreements such as that of the Pensioner Medical Service agreement, under which the majority of the future Australian Medical Association members are obliged to work. This agreement contains no protection from the effects of inflation. We must never again find ourselves in the position that our elected representatives are able to sign away our future security on the glib and plausible "reassurance" of a politician.

The above examples refer to the Federal sphere. Similar situations do arise within the State as over relations between doctors and hospitals, social services and other State public health matters. Often these changes are immaterial to those of us who have the time to participate in medical politics at the executive level. It would seem oft-times in the eyes of this relatively small group of the profession that the changes will be beneficial. If the regulations governing these changes were made known to the adversely affected members of the profession when tabled in the House and before they become undisputed law, they could advise the Council accordingly. Council can then act at a time when its efforts could be of some avail—that is, before the regulation has become operative.

Those of us who are to be the foundation members of the Australian Medical Association must ensure that there shall be an indisputable safeguard for the rank and file of the profession, both for itself and for its relationship with the community.

Yours, etc.,

RONALD B. WILES.

Lindfield Medical Centre,
280 Pacific Highway,
Lindfield, N.S.W.
February 27, 1961.

SIR: Delegates from local associations were not authorized to approve of the new constitution for the proposed new medical association of Australia. The Convention was not empowered to do so either. But the New South Wales State Council exercised its legal right in certain regards. Apparently the only potential barrier to the careering chariot ridden so rapidly by those who are determined to see the new constitution a reality, is a forthcoming meeting of the Federal Council in two-three weeks' time.

More delegates to the Convention than one can swear as to: (*a*) their own confusion; (*b*) their local association's understanding that all deliberations were to be tentative; (*c*) their surrender of their local association's options to consider further the proposed constitution, which occurred when they acquiesced in committing their local associations on the grounds that there was no time for the latter to meet again to consider the constitution. In a not altogether dissimilar way was the profession in Britain nationalized.

We do not argue the merits of nationalization; but we do hold that it is the view of the electorate: (*a*) that, to an undesirable degree and in an undesirable way, it has been disenfranchized; (*b*) that it prefers democracy to dictatorship; (*c*) that it accepts the delay and expense necessary adequately to ascertain and implement its wishes; (*d*) that it holds principle more important than expediency.

Yours, etc.,

R. I. MEYERS.

(Written in a purely private capacity.)

64 Clanville Road,
Roseville,
New South Wales.
February 25, 1961.

AN INTRODUCTION TO THE McWHIRTER CONTROVERSY.

SIR: I would be grateful for the opportunity to offer a few comments regarding the article published on February 25, 1961, by Mr. W. W. Woodward concerning "the McWhirter Controversy". The whole clinical series, which covers a ten-year period, is now referred to in Edinburgh as "the McWhirter Experiment". It involved cooperation between the various departments of the Edinburgh public hospitals, and was the result of general dissatisfaction with the end results of accepted methods of treating carcinoma of the breast.

The surgical authorities in Edinburgh will readily admit that simple mastectomy and radiation is not the treatment of choice for Stage I and Stage II cases, but they feel that a genuine attempt has been made by their departments to improve the general standards of treatment of a disease for which the surgical world has no adequate answer.

Yours, etc.,

ARTHUR P. CRAWFORD.

Wickham House,
Wickham Terrace,
Brisbane.
March 2, 1961.

CONSCRIPTION OF MEDICAL OFFICERS.

SIR: Understaffing of Cairns Base Hospital (or any other rural hospital) is usually due to: (i) absence of legislation providing adequately for graduate training of R.M.O.'s; (ii) absence of provision for study leave on pay; (iii) absence of Treasury action to provide salaries for the extra posts necessary; (iv) lack of a firm arrangement whereby registrars of city teaching hospitals, as part of their conditions, are required to serve for three to six months out of their four to five years seconded to rural hospitals.

Understaffing may be solved by conscription—but "the profession" is not to blame for the socio-economico-political ills which surround it. A Queensland medical parliamentary university senator once stated that the British Medical Association was a voluntary body with very little real power.

However much fire exists under that smoke, it is good to reflect upon the current work of the Post-Graduate Federation, especially in relation to graduate training and the staffing of country and city hospitals. Much needs to be done, with little time to do it in.

Yours, etc.,

R.M.

Sydney.
March 4, 1961.

SIR: The recent correspondence in THE MEDICAL JOURNAL OF AUSTRALIA under the title of "Conscription of Medical Officers" calls for some explanation. The letter from the Secretary, Hospitals Commission of New South Wales, in the issue of your Journal of February 4, gives a broad outline of the method of appointment of junior resident medical officers to hospitals in New South Wales, but the following remarks may help to clarify the position.

At the commencement of the final degree examination, each candidate is given a list of hospitals requiring resident medical officers. The candidate is invited to indicate his order of preference for appointment, and he is given about four weeks in which to return the form. He may alter his preferences—as is often done—right up to the day of appointment, some three weeks after the date set down for the return of the form.

Each year, and generally on the day of the last written paper, the candidates are addressed by the Medical Secretary of the New South Wales Branch of the British Medical Association. On the last occasion the writer addressed them and stressed that the Committee for Placement of Resident Medical Officers held that as a graduate's appointment would be made in accordance with: (*a*) his position on the order of merit issued by the University of Sydney, and (*b*) his list of preferences, he should not refuse the appointment given him, unless he could arrange with another graduate to change appointments and obtain the support of the Committee to this arrangement.

To refuse an appointment has two unfortunate results, viz.: (*a*) it deprives some other candidate, who is appointed to a hospital of a lesser preference, from obtaining the particular hospital; (*b*) it lessens the number of resident medical officers which the Committee has seen fit to allocate to a hospital. Once hospitals have been notified of all appointments, the aforementioned situations cannot easily be rectified.

In the particular case responsible for the correspondence, the successful candidate was two-thirds of the way down in the order of merit list, but was successful in obtaining an appointment which was his seventh choice. In this regard it is to be noted that his first four preferences were for the teaching hospitals. He had ample opportunity to alter his list of preferences if he so desired. He did not do so but refused his appointment and, subsequently, accepted an appointment at a hospital which was his twenty-fourth preference.

The wording of the letter from the Secretary of the Hospitals Commission was unfortunate, but the profession can rest assured that as far as the Committee is concerned, allocation of junior resident medical officers will continue to be on the basis of their preferences and order of merit. It is expected of them, however, that once having been appointed in accordance with such preferences and their positions in the order of merit, they will accept their appointments. Failure to do so would be unfair to their colleagues and the hospitals and would create unnecessary difficulties for the Committee in its work.

Yours, etc.,

HUGH HUNTER,
Deputy Medical Secretary,
New South Wales Branch of the British Medical Association.

135 Macquarie Street,
Sydney.
March 8, 1961.

Public Health.

VACCINATION AGAINST INFLUENZA.

THE following set of recommendations has been made available to us by Dr. P. L. Bazeley, Director of the Commonwealth Serum Laboratories. This was prepared by the United States Public Health Service Advisory Committee on Influenza Research, under the chairmanship of Dr. T. H. Francis. It is an authoritative document which we reprint here for the information of the medical profession.

Recommendations for Vaccination against Influenza in the Civilian Population.

Experience with Asian influenza between 1957-1960 has served to re-emphasize that patients in certain disease categories who acquire influenza are at much greater risk of death or severe morbidity than the normal population or patients with miscellaneous diseases. In order to reduce the hazard to patients at high risk, *it is recommended*, if not previously immunized with a polyvalent vaccine, that they may be given two doses of polyvalent influenza vaccine during this summer and fall, as specified below.

If previously immunized with a polyvalent vaccine, *it is recommended* that a single dose of polyvalent vaccine be given to them during the fall prior to November 1st.

Furthermore, because the occurrence and the severity of influenza cannot be predicted accurately from year to year, annual immunization of patients at high risk *is recommended.*

Patients in the following disease categories apparently have experienced the highest mortality rates, and therefore, specific protection is clearly indicated for them as a routine practice.

A. Persons at all ages who suffer from chronic debilitating disease, e.g., chronic cardiovascular, pulmonary, renal or metabolic disorders; in particular:

1. Patients with rheumatic heart disease, especially those with mitral stenosis.

2. Patients with other cardiovascular disorders such as arteriosclerotic heart disease and hypertension, especially those with evidence of frank or incipient cardiac insufficiency.

3. Patients with chronic bronchopulmonary-disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, pulmonary tuberculosis.

4. Patients with diabetes mellitus.

5. Patients with Addison's disease.

B. Pregnant women.

In years of expected high incidence vaccination *is recommended* for the following groups of people:

1. The very young or old, i.e., aged three months to one year and persons over 70. The highest age specific death rates from influenza and pneumonia occur in these age groups.

2. Persons in medical and health services, public safety, public utilities, transportation, education and communications.

3. Persons in the age groups in which influenza occurs in highest incidence, namely 5 to 25 years.

Dose and Schedule of Vaccination by Age.

1. *Children three months old to pre-school age*: Initial doses of 0·1 to 0·2 ml. (50 to 100 CCA units) should be administered subcutaneously on two occasions, separated by one or two week intervals. A "booster" inoculation of the same strength should be given two to three months later. Preferably the schedule of vaccination should be completed by November 1.[1] Since febrile reactions to vaccine in this age group may reach an incidence of 20 per cent., it is suggested, when not contraindicated, that acetylsalicylic acid (one grain per year of age) be given every 6 hours for the first 24.

2. *Children aged 6 to 12 years of age*: 0·5 ml. (250 CCA units) should be administered subcutaneously on two occasions. Each dose should be separated by two or more months. Preferably the first dose should be given no later than August 1[1] and the second no later than November 1.[1]

3. *Adults (i.e., individuals 13 years of age or older)*: 1·0 ml. (500 CCA units) should be administered subcutaneously on two occasions, separated by two or more months. The schedule recommended for the two dose program in this age group is the same as in paragraph two.

4. *Persons previously immunized with polyvalent vaccine*: Each fall, prior to November 1,[1] persons previously immunized with polyvalent influenza virus vaccine should be reinoculated with a single dose according to the following schedule:

Children 3 months old to pre-school age: 0·1 to 0·2 ml.

Children aged 6 to 12 years: 0·5 ml.

Adults: 1 ml.

The Royal College of Obstetricians and Gynaecologists.

NEW SOUTH WALES STATE COMMITTEE.

THE New South Wales State Committee of the Royal College of Obstetricians and Gynæcologists announces that Dr. T. M. MacGregor, F.R.C.S.E., F.R.C.O.G., Consultant Obstetrician and Gynæcologist to the Western General Hospital, Edinburgh, and Sims-Black Professor for the Royal College of Obstetricians, will be in Sydney from April 12 to 26, 1961, and will give the following lectures: April 13, 2 p.m., St. Vincent's Hospital, "The Significance and Mechanism of Menstruation"; April 18, 2 p.m., Royal Hospital for Women, "Hypertensive Diseases in Pregnancy"; April 19, 2 p.m., Women's Hospital, Crown Street, "The Clinical Aspects of Some Abnormal Chromosome Patterns"; April 20, 2 p.m., Sydney Hospital, "The Significance and Mechanism of Menstruation"; April 20, 8 p.m., Stawell Hall, "Some Common Gynæcological Disorders"; April 21, 1.15 p.m., Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital, "Hypertensive Disorders in Pregnancy"; April 24, 2 p.m., Royal North Shore Hospital, "Primary Amenorrhœa—A Basic Problem".

Dr. MacGregor will be in Canberra on April 14, 15 and 16, and on April 16 will lecture on "Perinatal Mortality" and "Hypertensive Disorders".

All members of the medical profession are invited to attend Dr. MacGregor's lectures.

Medical Practice.

POLICE OFFENCES (AMENDMENT) ACT, 1908, OF N.S.W. AS AMENDED.

THE following notice appeared in the *Government Gazette of the State of New South Wales*, No. 27, of March 3, 1961.

POLICE OFFENCES (AMENDMENT) ACT, 1908, OF N.S.W. AS AMENDED.

Withdrawal of Authority to be in Possession of Drugs.

It is hereby notified for general information that under the provisions of Regulation No. 25 of the Police Offences (Amendment) Act, 1908, as amended, the authority of Mr. George William Berkeley, 288 Marrickville-road, Marrickville, as a Pharmacist to manufacture, retail, compound and dispense drugs to which the Act applies, is withdrawn as on and from Monday, 20th March, 1961. (A. 56-2,121).

C. A. KELLY, Chief Secretary.

[1] These dates apply to the northern hemisphere and will need adjustment in Australia.

NATIONAL HEALTH ACT.

THE following notices are published in the *Commonwealth of Australia Gazette*, No. 21, of March 2, 1961.

NATIONAL HEALTH ACT 1953-1959.

Notice in Pursuance of Section 134A.

Notice is hereby given that the Medical Services Committee of Inquiry for the State of Western Australia, after investigation, having reported on the 28th day of November, 1960, concerning the conduct of Arthur John Blofeld-Moody of 685 Beaufort-street, Mount Lawley, a medical practitioner, in relation to his provision of medical services under Part IV of the National Health Act 1953-1959, I, Donald Alastair Cameron, Minister of State for Health, did on the second day of February, 1961, reprimand the said Arthur John Blofeld-Moody.

Dated this second day of February, 1961.

DONALD A. CAMERON,
Minister of State for Health.

Notice is hereby given that the Medical Services Committee of Inquiry for the State of Western Australia, after investigation, having reported on the 28th day of November, 1960, concerning the conduct of Alexander Breckler of 685 Beaufort-street, Mount Lawley, a medical practitioner, in relation to his provision of medical services under Part IV of the National Health Act 1953-1959, I, Donald Alastair Cameron, Minister of State for Health, did on the second day of February, 1961, reprimand the said Alexander Breckler.

Dated this second day of February, 1961.

DONALD A. CAMERON,
Minister of State for Health.

Post-Graduate Work.

ST. VINCENT'S HOSPITAL, SYDNEY: GASTRO-ENTEROLOGY UNIT.

THE next meeting of the Gastro-Enterology Unit of St. Vincent's Hospital, Sydney, will be held on Thursday, March 30, at 5.30 p.m. Mr. J. Rankin will speak on "Fulminant Ulcerative Colitis". All medical practitioners are invited to be present.

SURGICAL SEMINARS AT ST. VINCENT'S HOSPITAL, SYDNEY.

A SURGICAL SEMINAR will be held in the fifth floor Lecture Theatre, St. Vincent's Hospital, Sydney, on Monday, April 3, 1961, at 5.15 p.m. Mr. T. Nash will discuss "Results with Billroth I Gastrectomy".

Notes and News.

Trends in Juvenile Delinquency.

In Public Health Papers No. 5, published by WHO, Professor T. C. N. Gibbens, of the London University Institute of Psychiatry, and WHO Consultant, states that television, radio, Press and cinema have often been held responsible for the increase in juvenile crime and violence. They are easy to accuse, because any member of the public can form an opinion by merely turning a knob, while it will take some time to experience the effect of any particular club or cafe. He holds that these media may determine the content of, but do not motivate, offences of juvenile

delinquents. Pointing out that traditional nursery stories are often thought today to be brutal and frightening, Professor Gibbens states that the realism of many modern programmes may be accepted as "conventional" by modern youth. "It may be sounder", he writes, "to condemn certain programmes as beneath human dignity, rather than to blame them for having specific results, since Press, T.V. and radio do not appear to motivate offences although they may determine their content."

There is a widespread view that a "good" and "healthy" society should not have any delinquency. No doubt this is ideal, but as long as parents are unstable and the young as experimental as they are, it is questionable, Professor Gibbens considers, whether the elimination of delinquency, even if it was possible, is really desirable. There is much to indicate that delinquency may represent a valuable safety valve.

One biological feature, which has aroused a good deal of interest, is that youths of many countries are reaching their maximum height at an earlier age. Lately, the average age of puberty has also been going down at the rate of about six months per 10 years. These changes are generally related to better nutrition. At the same time, the tendency is to regard young people as psychologically immature to a higher age than formerly. The possible significance of the widening gap between early physical maturity and later psychological maturity is being freely discussed.

The belief that dishonesty or hooliganism is wrong is usually widely and firmly adhered to by parents of delinquents, and apparently by most other sections of the community. To explain how such hooliganism originates and what purpose it serves, what preserves it and transmits it, Professor Gibbens cites "one of the most complete statements of the findings of sociology and social psychology". The delinquent feels that he has an inferior status in the wider community; the delinquent group restores his standing, because it denies the values of the wider community. Such an attitude would call for the formation of gangs or hooligan groups.

Dr. Gibbens stresses the importance of a correct interpretation of the statistics that purport to show a great increase of juvenile delinquency throughout the world. A rise in the incidence may be due to changes in methods of detecting offences, or to the police arresting and charging people for offences they previously ignored, or to changes in the law creating offences where offences did not formerly exist, or to changes in the action of the courts, or to changes in the collection or interpretation of statistics. Clearly, for example, the incidence of delinquency will differ if it is defined as beginning variously at the age of 8, 13, 14 or 15 years, as in fact it is in different countries.

Fourth World Congress of Cardiology.

The Fourth World Congress of Cardiology will be held on October 7 to 13, 1962, at Mexico City. The Secretary General wishes to know as early as possible the approximate number of people who propose to attend the Congress. Further information may be obtained by writing to the Secretary General, IV World Congress of Cardiology, Instituto N. de Cardiologia, Avenida Cuauhtemoc 300, Mexico 7, D.F.

International Psychosomatic Cancer Study Group.

The Second International Conference of the International Psychosomatic Cancer Study Group will be held from August 27 to 29, 1961, in Paris. The theme of the conference will be "Psychosomatic Aspects of Neoplastic Disease". Further particulars may be had from the United Kingdom representative, Dr. D. M. Kissen, Brookfield, Elm Walk, Bearsden, Glasgow, Scotland.

Reunion of December, 1936, Melbourne Medical Graduates.

A twenty-five year reunion of the December, 1936, Melbourne medical graduates is to be held late in 1961 or early in 1962. Those interested, who are likely to be in Melbourne about that time, are asked to notify Dr. Norman Long, 627 Malvern Road, Toorak, S.E.2, Melbourne, indicating their most suitable times.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED FEBRUARY 11, 1961.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	3(1)	1	1	..	..	..	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1	..	..	..	..	..	3	..	4
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	5	12(7)	9(7)	..	..	..	2	1	29
Diphtheria	..	..	1(1)	..	1	..	..	..	2
Dysentery (Bacillary)	..	..	..	..	..	..	..	..	..
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	183(105)	46(23)	17(8)	41(17)	8(6)	3	1	2	301
Lead Poisoning	..	..	2	..	..	..	..	..	2
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	6	..	..	..	..	..	6
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	1	..	..	..	..	..	..	1
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	2	..	..	2
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	1	1(1)	1	7(4)	..	..	..	10
Salmonella Infection	..	..	..	..	3(2)	..	..	..	3
Scarlet Fever	1(1)	8(4)	1	..	..	..	..	..	10
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	1	1(1)	..	..	..	3
Trachoma	..	..	..	..	..	..	4	..	4
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	63(41)	12(10)	18(7)	1(1)	1(1)	3(2)	..	1	99
Typhoid Fever	..	1(1)	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	1(1)	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Corrigendum.

FURALTADONE—A CLINICAL TRIAL.

IN the paper entitled "Furaltadone—A Clinical Trial", by R. McEwin and J. Marsh, which was published in the issue of the Journal of March 4, 1961, the following sentence appears in the Addendum (page 319, second column, last paragraph):

> McCabe *et alii* (1960) conclude that their "results" permit no confidence in furaltadone as treatment for serious staphylococcal infections in the majority of patients".

The incorrect insertion of quotation marks after the word "results" alters the whole sense of the word and, as the authors of the paper point out, could give the impression that they consider the results of McCabe *et alii* inaccurate. We apologize for this typographical error.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Tziniolis, John, M.D., 1951 (Univ. Athens), licensed under Section 21 c (4), 7 Campbell Avenue, Paddington.

Moran, Clement Charles, M.B., B.S., 1959 (Univ. Sydney), 23 Saxon Street, Belfield.

Morgan, Bruce Alexander, M.B., B.S., 1956 (Univ. Sydney), 511 Old South Head Road, Rose Bay.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Burns, Richard John, M.B., B.S., 1959 (Univ. Adelaide), 8 Valmai Avenue, Kings Park.

Jellett, Leon Barry, M.B., B.S., 1959 (Univ. Adelaide), 33 Hendrie Street, Parkholme.

Evans, David Denton Edward, M.B., B.S., 1959 (Univ. Adelaide), 145 Goodwood Road, Goodwood.

Mattner, Charles Prince, M.B., B.S., 1959 (Univ. Adelaide), Woodside, Adelaide.

Shen, Edward. M.B., B.S., 1960 (Univ. Adelaide), Royal Adelaide Hospital, North Terrace, Adelaide.

Gilligan, John Eugene, M.B., B.S., 1960 (Univ. Adelaide), 23 Glanton Street, West Hindmarsh.

Young, James Fairbairn, M.B., B.S., 1960 (Univ. Adelaide), 68 Statenborough Street, Erindale.

Alpers, Michael Philip, M.B., B.S., 1960 (Univ. Adelaide), 20 Stannington Avenue, Marryatville.

Lane, Lionel Harold Davies, M.B., B.S., 1960 (Univ. Adelaide), 3 Alexandra Avenue Rose Park.

Leeson, Dorothy Jean, M.B., Ch.B., 1942 (Univ. London), 28 Power Street, Mount Gambier.

Holbrook, Judith Mary, M.B., B.S., 1957 (Univ. London), 24 Hogarth Grove, Elizabeth Grove.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

O'Moore, Ellenora Patricia, M.B., B.S., 1960 (Univ. Adelaide); Cox, David William, M.B., B.S., 1960 (Univ. Adelaide); Martinkus, Sagitis, M.B., B.S., 1960 (Univ. Adelaide); Woolcock, Ann Janet, M.B., B.S. (University of Adelaide); Kimber, Richard John, M.B., B.S., 1960 (Univ. Adelaide); Vorbach, Adrian Neil, M.B., B.S., 1960 (Univ. Adelaide); Robson, Kenneth James, M.B., B.S., 1960 (Univ. Adelaide); Andersen, Graham John, M.B., B.S., 1960 (Univ. Adelaide); Edgar, Melvin Lawson, M.B., B.S., 1960 (Univ. Adelaide); Sando, Brian Gordon, M.B., B.S., 1960 (Univ. Adelaide); Ng, Robert Lian Wee, M.B., B.S., 1960 (Univ. Adelaide); Whiting, John Harold, M.B., B.S., 1960 (Univ. Adelaide); Kearney, Geraldine Helen Elizabeth, M.B., B.S., 1960 (Univ. Adelaide); Murray, Lyndon George, M.B., B.S., 1960 (Univ. Adelaide); Strickland, Robert Geoffrey, M.B., B.S., 1960 (Univ. Adelaide); Fraser, George McLennan, M.B., B.S., 1955 (Univ. London); Osmond, Ruth, M.B., B.S., 1942 (Univ. Adelaide).

Deaths.

KENNETT.—George Hedley Kennett, on March 6, 1961, at Goulburn, N.S.W.

Diary for the Month.

MARCH 21.—New South Wales Branch, B.M.A.: Council Quarterly.
MARCH 22.—Victorian Branch, B.M.A.: Branch Council.
MARCH 23.—New South Wales Branch, B.M.A.: Annual Meeting.
MARCH 24.—Queensland Branch, B.M.A.: Council Meeting.
MARCH 28.—New South Wales Branch, B.M.A.: Council (Election of Officers).

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full data in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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